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(54) Tamponade

(57) Die Erfindung betrifft eine Tamponade zur resorbierbaren, volumenaktiven Wundhöhlenprotektion, vorzugsweise aus mit einem Polyurethan-Strukturweichschaum-Stützgerüst cogeschäumten, resorbierbarem Kollagenschaum mit inkorporierten resorbierbaren, permeablen Hohlfaseranordnungen bestehend, die es gestattet, bei durch operative Eingriffe entstandenen Wundhöhlen einerseits eine gekoppelte aktive/passive Wundversorgung durchzuführen, andererseits aber auch in diesen Wundhöhlen eine gesteuerte Rekonstruktion mit körpereigenem Gewebe zu erreichen.

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Beschreibung

Die Erfindung betrifft eine Tamponade zur resorbierbaren, volumenaktiven Wundhöhlenprotektion, vorzugsweise aus mit einem Polyurethan-Strukturweichschaum-Stützgerüst cogeschäumtem, resorbierbarem Kollagenschaum mit inkorporierten resorbierbaren permeablen Hohlfaseranordnungen bestehend, die es gestattet, bei durch operative Eingriffe entstandenen Wundhöhlen einerseits eine gekoppelte aktive/passive Wundversorgung durchzuführen, andererseits aber auch in diesen Wundhöhlen eine gesteuerte Rekonstruktion mit körpereigenem Gewebe zu erreichen.

Es sind Schaumstrukturen (DD-WP 33 1 817 OE A61F 2/02) bzw. texturierte mä-anderförmige Strukturen (EP 02 59 536 A **2**) bekannt, die jedoch nicht für eine temporäre Wundhöhlenprotektion geeignet sind, da sie entweder infolge der verwendeten Werkstoffe und Konstruktionsprinzipien zu unflexibel oder nicht resorbierbar sind, demzufolge durch den Chirurgen des öfteren gewechselt werden müssen und infolge ihrer relativen Steifigkeit zu mechanisch bedingten Reizungen im Wundbereich führen.

Der Erfindung liegt die Aufgabe zugrunde, ein Gebilde für eine resorbierbare, volumenaktive Wundhöhlenprotektion zu schaffen, das dem Chirurgen einerseits die kontinuierliche sterile und nichtinvasive Entfernung von Exsudat ermöglicht und andererseits eine kontinuierliche Wirkstoffabgabe, wie z. B. Antibiotika, gestattet. Zusätzlich wird durch die temporäre Stützfunktion der resorbierbaren volumenaktiven Wundhöhlenprotektion ein Einwachsen von körpereigenem Gewebe ohne eine traumatische Druckerhöhung in der Wundhöhle ermöglicht, indem sich ein Gleichgewichtszustand zwischen Gewebewachstum und Resorption des Stützschaumes einstellt.

Das Ziel der Erfindung besteht darin, daß durch Anwendung einer kompatiblen porösen und vor allem weitgehend resorbierbaren Stützeinlage in der Form eines Strukturweichschaumkomposites mit eingelagerten, ebenso resorbierbaren semipermeablen Hohlfasern, sowohl eine Möglichkeit der Dauerspülung der Wundhöhle mit passiver oder aktiver Drainage nach außen geschaffen wird, als auch die Rekonstruktion der Wundhöhle durch nachwachsendes körpereigenes Gewebe zu unterstützen. Weiterhin soll durch die Stützfunktion des Weichschaumkomposites ein Kollaps der Wundhöhle verhindert werden bis diese vollständig im Laufe des Heilungsprozesses durch körpereigenes Gewebe ausgefüllt wurde. Die Aufgabe wird erfindungsgemäß durch die in Anspruch 1 genannten Merkmale gelöst. Der Vorteil der entwickelten resorbierbaren volumenaktiven Wundhöhlenprotektion besteht darin, daß dem Chirurgen die als räumliche Gebilde wie z. B. in Halbkugel-, Hantel- oder Wetzsteinform dergestalt vorkonfektioniert angeboten werden, so daß intraoperativ dem Chirurgen die Möglichkeit eröffnet wird, ohne Funktionsverlust einen paßgenauen Zuschnitt vorzunehmen.

Weiterhin können durch die eingeschäumten resorbierbaren Hohlfasern sowohl gezielte Medikamentenzugaben, als auch aktive und passive Abscheidungen von Wundhöhlenflüssigkeiten erfolgen.

Ein Ausführungsbeispiel der Erfindung ist im folgenden anhand einer Zeichnung näher dargestellt und beschrieben worden.

Es zeigen:

Fig. 1 Schnittansicht einer Tamponade,

Fig. 2 Einzelheit X nach **Fig.** 1 der Tamponade im vergrößertem Maßstab.

Gemäß **Fig.** 1 befinden sich in der Tamponade **1** eingeschäumte, resorbierbare Hohlfasern **2** die mit ihrem einem Ende in Richtung der äußeren Begrenzung ausgerichtet sind, so daß beim endgültigen Zuschneiden durch den Chirurgen unter OP-Bedingungen die Funktionalität erhalten bleibt. Das zweite Ende der resorbierbaren Hohlfaser **2** ist gebündelt über einen resorbierenbaren Schlauch **3** mit der Außenwelt verbunden.

Gemäß **Fig.** 2 sind in einem offenzelligen Polyurethanweichschaumstützgerüst **4**, das einen resorbierbaren Weichschaum **5** umschließt, resorbierbare Hohlfasern **6** eingeschäumt.

Darstellung der verwendeten Bezugszeichen

1 Tamponade
2 resorbierbares Hohlfaserbündel
3 resorbierbarer Schlauch
4 offenzelliges Polyurethanweichschaumstützgerüst
5 resorbierbarer Weichschaum
6 semipermeable resorbierbare Hohlfaser

Patentansprüche

1. Tamponade für eine resorbierbare volumenaktive Wundhöhlenprotektion, **gekennzeichnet dadurch,** daß räumliche oder flächige Strukturweichschaumgebilde (**1**) ein Weichschaumstützgerüst (**4**) besitzen, das von einer resorbierbaren, vorzugsweise Kollagenweichschaumeinlage umhüllt ist, in die ebenfalls resorbierbare semipermeable Hohlfasern (**6**) eingebettet sind, so daß ihre inneren Enden zu einem Hohlfaserbündel (**2**) zusammengeführt sind und das Hohlfaserbündel (**2**) mit einem zu bzw. abführenden Schlauch (**3**) verbunden ist.

2. Tamponade nach Anspruch 1, gekennzeichnet dadurch, daß das Strukturweichschaumgebilde (**1**) aus 5 – 10% tragendem offenzelligen Polyurethanweichschaum und 90 – 95% resorbierbaren Weichschaum mit eingeschäumten ebenfalls resorbierbaren Hohlfasern (**6**) besteht.

Hierzu 1 Seite(n) Zeichnungen

— Leerseite —

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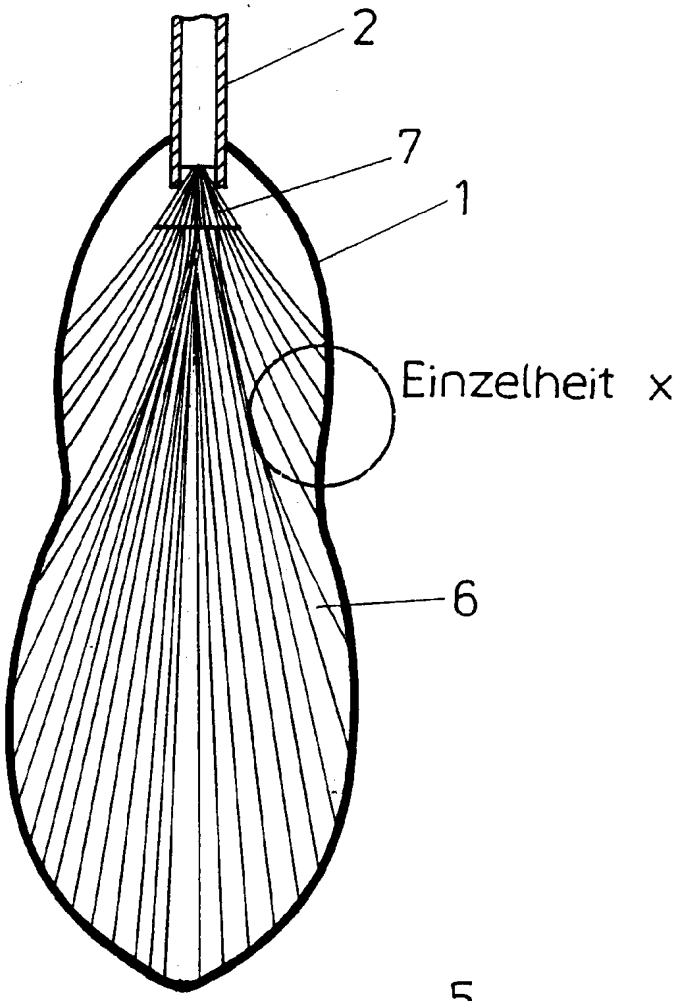

Fig. 1:

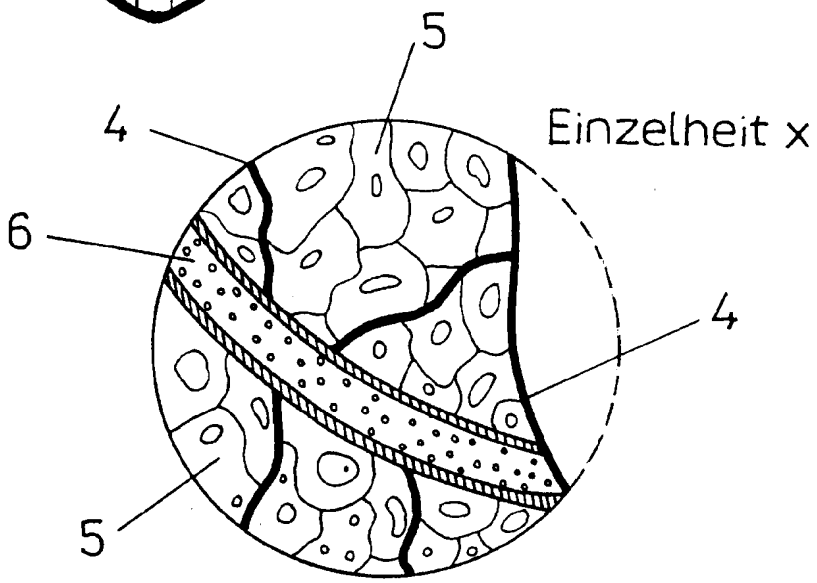

Fig. 2:

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(54) Title: METHODS AND APPARATUS FOR APPLICATION OF MICRO-MECHANICAL FORCES TO TISSUES

(57) Abstract: Methods and devices for transmitting micromechanical forces locally to induce surface convolutions into tissues on the millimeter to micron scale for promoting wound healing presented. These convolutions induce a moderate stretching of individual cells stimulating cellular proliferation and elaboration of natural growth factors without increasing the size of the wound. Micromechanical forces can be applied directly to tissue, through biomolecules or the extracellular matrix. This invention can be used with biosensors biodegradable materials and drug delivery systems. This invention will also be useful in pre-conditoned tissue-engineering constructs *in vitro*. Application of this invention will shorten healing times for wounds and reduce the need for invasive surgery.

METHODS AND APPARATUS FOR APPLICATION OF MICRO-MECHANICAL FORCES TO TISSUES

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of United States Provisional Application No. 60/291,120, filed May 15, 2001, the entire disclosure of which is hereby incorporated by reference.

FIELD OF THE INVENTION

[0002] The invention relates to the promotion of tissue growth and wound healing in general and more specifically to the application of micro-mechanical forces to promote tissue growth and wound healing in mammals and in artificial tissue or tissue explants in vitro.

BACKGROUND OF THE INVENTION

[0003] Over one million new chronic wounds develop in the United States each year with estimated treatment costs of $7 billion. Scores of new wound healing products are developed annually, yet wounds continue to be a significant public health problem as our population ages and as rates of diabetes mellitus increase. Wounds can be conceptualized as defects in protective skin coverage. Without this physiological barrier, wounds desiccate and are invaded by microorganisms leading to potential infection, with progressive tissue and fluid loss. The inability to heal lower extremity wounds often leads to amputation. There are several etiologies for chronic wounds, including trauma, burns, radiation, venous stasis, chronic infection, and systemic diseases such as diabetes. Current methods for improving wound healing emphasize effective drainage, prevention of infection, reduction of inflammation and minimization of tissue and fluid loss.

[0004] Most chronic wounds are characterized by a loss of cells and connective tissue matrix from at least the outer layer of skin (epidermis) and often also from the lower layer of skin (dermis) and deeper structures such as fat, muscle and bone. Closure of large wounds requires the production billions of cells, nutrition through a vascular network and mechanical strength from proteins and glycosaminoglycans present in a nascent extracellular matrix (ECM). To date, most research on wound healing acceleration has focused on soluble growth factors (i.e. FGF, PDGF, TGF-β, VEGF) that naturally stimulate cell proliferation, migration, ECM deposition and angiogenesis. However, the application of cytokines to wounds remains difficult because of the

complex, concerted interaction between these factors and their very short half-life in vivo. Moreover, soluble chemicals alone fail to provide structural guidance to rebuild the tissue architecture.

[0005] Mechanical forces are well known to have a fundamental role in biologic systems. In development, forces of developing muscles affect bone formation. In addition the application of mechanical forces has been an important adjunct to surgery. Distraction osteogenesis allows gradual lengthening of bone. Tissue expansion allows gradual lengthening of soft tissues, including nerves and blood vessels. Tension wound-approximation devices close wounds over time. Application of sub-atmospheric pressure to wounds has been shown to increase the vascular supply within the wound and to accelerate healing. All of the above forces are directed at the wound in a single dimension and applied evenly over large areas (greater than 1 cm^2).

SUMMARY OF THE INVENTION

[0006] This invention relates to the development of devices that permit the application of micro-mechanical forces (MicMFs) to promote tissue growth and wound healing in mammals. The same technology may be used to promote the growth and development of artificial tissues or tissue explants in vitro. Given an aging population and the increasing prevalence of diabetes (a major cause of chronic wounds) this invention will find broad usage in health care for wound repair, tissue reconstruction, and potentially organ replacement. Accelerating wound healing reduces complications including infection, limb loss and pain. Secondary economic gains will result from reduced hospital stays, wound treatments, and medical care for chronically ill patients.

[0007] The paradigm for wound healing upon which the invention is based circumvents the daunting complexity of using the right mixture of growth factors at the right time by taking advantage of the observation that topological and mechanical force cues sensed by individual cells play a natural role in promoting cell proliferation according to local needs. Referring to Figure 1, ample cell culture experiments have demonstrated that MicMFs exerted on individual cells can switch on specific genes that cause cell proliferation and regulate various cell functions critical for tissue development. Such a control mechanism has been implicated in wound healing. The invention consists of a set of devices and methods that exploit these physical and local cues, in addition to growth factors, to enhance wound healing.

[0008] This disclosure will focus on the development of methods to locally concentrate and focus these mechanical forces on the micron to millimeter scale. The use of MicMFs will not only more efficiently deform cells and alter cell behaviors, such as growth, that are necessary for

optimal tissue growth and repair, but also do so without altering the macroscopic anatomy of the wound. Analysis of how forces are distributed within tissues using finite element analysis or advanced sensing technologies provides new data for precision engineering of devices that can be used in conjunction with conventional methods of macroscale force application (e.g., referring to Figure 2 use of tension, compression, shear, electromagnetic forces, pressure, osmotic, surface tension, gravity, etc.) to concentrate MicMFs locally and thus, to exploit this new mitogenic pathway for improved wound healing. These devices are capable of concentrating stresses locally to induce precise cellular strains while applying forces over large tissue areas and may be adapted to apply forces on a continuous or cyclical basis. This methodology is especially useful for promoting wound healing, however, it also may be useful for stimulating growth or pre-conditioning of tissues in vitro, for example, to increase the wall strength of artificial blood vessels created using tissue engineering approaches.

[0009] This invention relates to devices and related methods for concentrating mechanical stresses locally on the millimeter to micron scale and methods to apply these stresses to cells within living tissues. This may be accomplished by engineering materials that induce local convolutions in the wound surface, topographic changes in the extracellular matrix that secondarily stretch cells, or direct deformation of cells that adhere to the device. These micro-mechanical strains stimulate wound healing by promoting cellular proliferation and migration, elaborating of natural soluble growth factors, and stimulating angiogenesis. The invention may comprise one or more of the following steps: coating micro-mechanical devices with extracellular matrix (ECM) factors, peptide fragments, synthetic molecules and growth factors to enhance cell proliferation, cell adhesion, and wound healing, combining MicMFs with exogenous growth factors and cytokines, optimization of MicMF application and drug delivery with mathematical modeling and feedback control, simultaneous localized and controlled delivery of drugs, proteins, and other factors to control edema, minimize infection and inflammation, and facilitate wound healing, employing the design of biodegradable, "smart-material" based devices that allow transmission of optimal MicMFs as they degrade, and fabrication of materials with micron to millimeter sized features, such as pores, which locally concentrate stress on adherent cells when forces are applied over large areas of the material.

[0010] The invention is based on the scientific insight that MicMFs play an important role in controlling cell proliferation. The presence of soluble growth factors alone does not optimize cell proliferation. For optimal proliferation, adherent cells, such as fibroblasts and endothelial cells, need to be stretched. Moreover, several forms of mechanical forces (i.e. stretch, turbulent

flow shear stress, distortion, pressure, etc.) stimulate cell growth, migration, and other biochemical changes necessary for tissue growth and repair. Thus, forces applied to individual cells are critical in governing their response to soluble cytokines and ECM molecules. Physiologically, the non-muscle actin-myosin apparatus generates an isometric tension of the cytoskeleton. This process requires an ECM substrate (to which the cell is attached) that resists the "shortening" of the cell, thus allowing intracellular tension to build up to levels which are critical for cell growth.

[0011] In one embodiment, the invention relates to a device containing a material that contains multiple pores which when mechanically distorted concentrates stresses locally and focuses these micromechanical forces on adjacent living cells to promote their growth within living tissues. In one embodiment the pores are greater than 1 micrometer and less than 1 centimeter, and preferably greater than 20 micrometers and less than 2 millimeters. In another embodiment, the invention is constructed from non-degradable polymers including but not limited to polyurethane and polydimethylsiloxane. In another embodiment, the invention is constructed from biodegradable polymers including but not limited to collagen, fibrin, PLA, PGA, and PMA.

[0012] In other embodiments, pressure is applied through the application of vacuum or positive pressure. In another embodiment, the device is fabricated using microfabrication techniques, such as soft-lithography or conventional porous polymer fabrication strategies (e.g., salt leaching).

[0013] The invention also relates to a method of applying this above referenced materials to wounds or tissue grafts and exerting local mechanical distending forces at the micron to millimeter scale. These forces distend large regions (over 1 cm^2) of the material in order to accelerate tissue ingrowth and enhance tissue repair throughout the depth of the tissue without increasing the overall size or expanding the boundaries of the tissue (i.e., without causing wound opening or dehiscence). The invention also relates to a method of applying this device to promote growth and expansion of tissues in vitro by applying distending micromechanical forces throughout the depth of the tissue.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] Figure 1 is of block diagram indicating the generalized sequence of steps in an embodiment of the invention;

[0015] Figure 2 is a schematic diagram of cell distortion induced by extrinsic forces including tension, compression, shear, surface tension, pressure, osmosis and gravity;

[0016] Figures 3A through 3D are schematic depictions of a wound as a flat surface with induced convolutions for uniaxial corrugation, multidimensional convolution, and rotational shear;

[0017] Figure 4 is a block diagram indicating the sequence of integrated mechano-chemical wound healing acceleration according to an embodiment of the invention;

[0018] Figure 5 is a schematic isometric diagram of a micromechanical force device according to an embodiment of the invention;

[0019] Figures 6A through 6D depict a finite element analysis of an embodiment of a porous sheet applied to a wound in which sub-atmospheric pressure has been applied; and

[0020] Figure 7 is a block diagram indicating the sequence of a smart feedback control system according to an embodiment of the invention.

[0021] Figure 8A is a schematic cross-section of a wound bed with an application of one embodiment of a therapeutic device according to the invention.

[0022] Figure 8B is a schematic cross-section of a wound bed depicting tissue in-growth with the device of Figure 8A.

[0023] Figure 9 is a schematic isometric diagram of a wound bed with an application of one embodiment of a therapeutic device, depicting a filtration, recirculation and nutrient delivery system.

[0024] Figure 10A is a schematic cross-section of a wound bed with an application of one embodiment of a therapeutic device according to the invention depicting a wound sensor array.

[0025] Figure 10B is a schematic isometric diagram of a wound bed with an application of the device of Figure 10A.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[0026] Physical forces that are applied to tissues at the macroscale can trickle down to affect cell form and function. However, when these forces are applied homogeneously over large areas, the level of strain or deformation experienced by individual cells can be quite small, thus limiting the cellular response. In addition, global force applications typically result in a wide variety of stresses within a wound. Several devices are currently available that assist in wound healing by applying mechanical forces on the macroscale (evenly over areas greater than 1 cm^2) including tension wound closure devices, vacuum assisted closure and devices applied in distraction osteogenesis. This invention focuses on the development of methods and devices to locally concentrate forces applied on the macroscale within multiple smaller regions (less than 1 cm^2 and preferably less than 1 mm^2), so as to amplify the forces that are experienced by

individual cells on the microscale. One advantage of this method of MicMF application is the ability to induce cell stretch without increasing the size of the wound, thus minimizing the likelihood of wound dehiscence. One way to increase cell stretch is to create surface features within a device that induces three-dimensional convolutions within the wound. Accordingly, while exemplified in the following manner, the invention is not so limited and one skilled in the art will appreciate its wide range of application upon consideration thereof.

[0027] As depicted in Figures 3A through 3D, a wound can be conceptualized as a flat three-dimensional surface. Convolutions of the wound can be induced in a number of fashions including uniaxial corrugation, as depicted in Fig. 3B; multidimensional convolution, as depicted in Fig 3C; and rotational shear, as depicted in Fig. 3D. After inducing localized convolutions in the wound by MicMFs, individual cells are stretched to a greater degree along the convoluted surfaces, thereby increasing the surface area of cells on the wound surface, without an increase in the overall wound size. The degree of convolution is directly related to the amount of cell stretch.

[0028] The general principle for force transmission into cells is explained as follows. The invention induces local cell strain using devices that apply MicMFs to multiple micro-regions of the wound without global wound extension. ECM receptors on the cell surface, such as integrins, sense and transduce the MicMFs to the cytoskeleton. Therefore, ideally, the therapeutically applied forces should be directed to the ECM and their interconnected receptors and cytoskeletal linkages. A general principle to increase force transfer efficiency is to coat the force generating device with biomolecules that bind directly to ECM components (e.g., heparin, antibodies to ECM components, such as collagen) or molecules such as fibronectin or RGD peptides that bind directly to cell surface integrin receptors. In vitro work to date on a variety of cell types suggest that different cell types exhibit different sensitivities to mechanical strain in terms of their growth response; different regions of tissues and wounds also may exhibit different sensitivities to force. Conventional medical devices that use forces therapeutically apply a single level of stress homogeneously over larger areas of tissue. Thus, it would be a great advantage to have devices that could apply optimal levels of deformation in appropriate micro-regions of a tissue and at appropriate frequencies or that vary in the level of stress that they apply within different areas of a single wound. The current invention provides both of these functions.

[0029] MicMFs originate from intrinsic stresses within structural molecules and body movements that transmit forces via distinct anatomic structures down to the cellular scale.

Individual cells continuously perceive forces. MicMFs play an important role in governing cell proliferation and spatially orchestrating growth to meet tissue demand at the macroscopic. Thus, mechanical forces are key regulators of regeneration of functional tissue. Unlike the two-dimensional environment in which cell stretch pathways have been analyzed in vitro, cells in wounds exist in a complex three-dimensional network.

[0030] The physiology of fluids in the body can be divided into three compartments: 1) intravascular, 2) intracellular, and 3) extracellular. The intravascular component contains blood and its components and is responsible for the nutrition of other compartments through diffusion across capillary membranes. The extracellular compartment is comprised of structural extracellular matrix (ECM) proteins and glycosaminoglycans, salts and water. ECM proteins include several types of collagen, proteins (e.g., fibronectin, vitronectin and elastin). The ECM is in intimate contact with cells. Therefore, in vivo, MicMFs will often be transmitted through the ECM. In addition, the hydration state of the ECM will be a critical factor determining the magnitude and direction of forces transmitted to cells. For example, in edematous states, the ECM has excess water and swells. This can result in compression of the cells within the ECM making them less mitogenic. This can be seen in states such as lymphedma, venous stasis disease, burns and congestive heart failure. Application of forces that reduce edema will restore cells to their normal size and orientation resulting in cellular proliferation. The invention is directed at solving the challenge of minimizing wound dehiscence (separation) while maximizing mechanical stresses applied to individual cells on the micron scale within the depth of the wound. It provides methods and devices to improve and optimize wound healing by concentrating mechanical stresses exerted at the cell without having to increase macroscopic forces (such as overall stretch) applied to the whole issue that could compromise wound closure.

[0031] In generating and directing micromechanical forces to cells, the magnitude of forces must be controlled such that it is well in the physiological range. Most in vivo experiments suggest that maximum proliferative activity of cells that mediate wound healing – fibroblasts, endothelial cells, epithelium – occurs between 10 and 20 percent strain. This is important because wound healing is a dynamic process and local topology and cellular strains are expected to change in the course of healing. Therefore, the present invention involves development of devices or improvements in existing devices that concentrates stresses locally over multiple regions of a tissue surface in order to produce optimal cell deformation on the microscale. In an advanced design, the components that generate forces are integrated into a system with feedback

control involving control elements such as Bio-Sensors or self-adapting ("smart") materials to further adjust the degree of cellular strain within the wound over time (see Fig. 4).

[0032] Mechanical stresses such as (1) compression and tension, (2) shear, (3) differential pressure that are applied evenly over a large surface area may be locally concentrated and focused using devices designed and fabricated with appropriate microarchitectural features, such as micron to millimeter-sized pores with controlled geometry, according to the present invention. The local forces would be selectively applied to cells in wounds to produce the appropriate strains and rates of strain necessary for optimal growth and repair. Both strain and edema can also be controlled through manipulation of (4) Starling forces. In addition, (5) Bio-Sensors and smart polymers could continuously monitor the degree of wound healing and provide feedback to the force generating device, resulting in a continually optimized level of applied load and strain. To further promote wound healing, drugs (antibiotics, mitogens) can be locally delivered, and (6) local biomolecular modifications can be made to enhance cell adhesion. Each of these components of the invention are independent modules that can be combined to create final products designed to meet practical needs, such as portability to allow for patient ambulation.

[0033] Referring to Figure 5, one embodiment of the invention comprises a collagen sponge made primarily of Type I collagen using bovine Achilles heel or skin as a source. The pore size range of the sponge is 50 to 550 micrometers with a molecular weight between crosslinks of approximately 10,000 Daltons. The sponge is covered with a polyurethane occlusive dressing through which a tube exits that is connected to a vacuum of 50 to 200-mm Hg that is applied, continuously or cycled. The mechanical forces that are applied globally to the sponge surface are concentrated locally due to the geometric constraints of the pore shape, size and distribution. Over time, the intersticies within the mesh will be populated by vascularized outgrowths of tissue from the wound. The mesh acts as a temporary scaffold that is biodegraded over time as well as concentrate stresses locally. Every one to seven days, the sponge can be replaced and the process restarted. This device can be combined with a non-degradable sponge to transmit the sub-atmospheric pressure throughout larger wounds.

[0034] A clinical application of one embodiment of the device is shown in Figure 8A. A matrix of variable composition can be sized to the specific wound 100 is placed into the wound bed. The matrix includes a porous biodegradable matrix 105, a nondegradable sponge 110, and occlusive dressing 115, each applied in sequential layers to the wound 100. The pore size of the biodegradable matrix 105 is preferably between 50 and 1500 micrometers. Components of the different types of matrices, which are chosen depending on the characteristics of the wound may

include natural polymers such as collagen, elastin, fibronectin, and laminin as well as synthetic polymers such as polyglycolic or polylactic acid. There will be a number of predetermined matrix compositions available for selection based on the specific wound 100. The biodegradable matrix 105 can be placed under vacuum or pressured via pressure tube 120. The matrices can be layered as depicted in Figure 8B, one atop the other for deep wounds in a sequential manner as tissue ingrowth 127 occurs into the matrix with subsequent changes of the device.In this arrangement, the biodegradable matrix 105 further comprises a first matrix layer 125a and a second matrix layer 125b. The first matrix layer 125a would not be removed from the wound 100 during the healing process, but rather would become part of the wound 100, with native tissue in-growth over time.

[0035] Deep-layer strains can be introduced to wounds by the presence of a pressure gradient. Relative to the atmospheric pressure, the wound can be exposed either to a lower pressure (through the application of a vacuum) or to higher-pressure (through inflation of a sealed balloon) using currently available technologies, such as vacuum assisted closure and a tissue expansion device, respectively. Currently, pressure variations are usually applied globally with the whole wound subject to one pressure. The invention provides a method to concentrate these stresses locally, with specific areas of wounds subject to specific, and possibly different, pressures.

[0036] As an example of localized pressure application, an elastic sheet containing multiple small (less than 1 cm diameter and preferably less than 2 mm) pores can be affixed to the wound (e.g., using a surface coating of molecules that mediate ECM or cell adhesion) after which an applied vacuum stretches the exposed portions of the wound through the open pores of the sheet. In this system, the stiffness of the sheet needs to be greater than the stiffness of the wound, and the edges of the pores within the elastic sheet would be shaped appropriately to minimize trauma due to stretching. Alternatively, using high positive pressure, forces can be preferentially applied to the sheet and adherent cells relative to the neighboring non-adherent cells. With both methods, site-specific stretching can be accomplished with different pressures at different pores by varying pore size, shape and location. The shape and size of pores can be optimized using computer design and analysis to provide optimal concentrations of stresses locally. Flexible and rigid sheets containing pores with defined shape, size and location on the millimeter to submicron scales can be created using a variety of manufacturing methods, and microfabrication techniques including soft lithography. A "foam padding" adherent to the base elastic sheet can also be used for space filling and impact reduction. These materials can also be coated with

polymers to enable controlled local delivery of drugs. The pressure can be set at an optimal value, or can be cycled at some optimum frequency corresponding to the optimal rate of strain to achieve cell proliferation.

[0037] Finite element analysis (FEA) can be used to evaluate the design of our pressure-based, porous elastic sheet, wound healing device. FEA is used to solve boundary value problems where closed form analytic solutions may be intractable. A mathematical model is used to model the geometry at discrete points, and the boundary of the modeled points is loaded with the forces and constraints that define the boundary conditions. Equations are set up by the solver based on the geometry that relate points inside the structure to points involving the boundary conditions.

[0038] In this exemplary analysis, a linear, homogeneous, isotropic model was constructed. By linearity it is meant that the stress strain behavior is linear over the strain ranges imposed. Homogeneous implies that the material has the same (average) properties from one part to another. Isotropic implies that the material responds uniformly in all directions. By using a linear assumption on the stress-strain response characteristic, the solver uses a small strain assumption. Thus the results are approximate, and may be validated with a large strain analysis using the correct stress-strain curve.

[0039] Referring to Figures 6A to 6D, the wound modulus of elasticity, sheet geometry, and applied pressure were treated as variable parameters. A one-dimensional model with a geometry defined by the typical pore width distance between the fibers (about 0.5 to 2 mm) was constructed. The skin was modeled with a constant thickness of 1 mm. The results of the modeling indicate that pore size of about 1.4 mm and a pressure of about 0.016 N/mm2 is sufficient to strain multiple local regions of the wound between 10 percent and 20 percent, the target range that has been shown to optimize cell proliferation.

[0040] In another embodiment, the device includes a porous FDA-approved, non-biodegradable material 110 (e.g., polyurethane, polydimethylsiloxane), either in a sponge configuration or as a sheet with pores designed and engineered (sized, shaped, and distributed) so as to optimally concentrate mechanical stresses locally and thereby promote tissue ingrowth in non-healing wounds or tissue grafts. The material is overlayed with the occlusive dressing 115, which may comprise a non-permeable solid sheet (e.g., silicone sheet) to ensure a good pressure seal. Mechanical distending forces are applied to this material through a portable, mechanical pump device linked by a pressure tube 120 that inserts into occlusive dressing 115. In another embodiment the device is driven by existing vacuum or positive pressure pumps or systems.

This embodiment provides more rapid and complete wound healing; while allowing the patient to remain ambulatory.

[0041] In yet another embodiment the matrix material 105 may includes a porous FDA-approved, biodegradable such as collagen, PLA, PGA, PMA, or other suture material. The advantage of the biodegradable material is that the overlying silicon sheet "sloughs" off naturally as the polymer degraded thereby minimizing damage and tissue loss during each "dressing change". The integration of the polymer lattice with ingrown cells also accelerates mass-filling of the wound site. This material therefore shortens healing time, decrease morbidity, and provide a better cosmetic result.

[0042] Compression and tension may be useful for wound healing for various types of tissues. For instance, compression promotes bone healing and cartilage regeneration, whereas tension might be more helpful in soft tissue healing and osteogenesis. Neither compression nor tension results in a "purely" compressed or stretched state for the cell however. The tensegrity model of cellular architecture implies that because of the networked organization of the cytoskeleton, tension in one direction may induce compression in subcomponents within the cell, such as microtubules. Compression in one direction may induce extension and tension other structural components (e.g., microfilaments) within the cell. Stretching of cell surface adhesion receptors and cytoskeletal components alters cellular biochemistry and regulates genes for replication.

[0043] Cells within the wound can be subjected to a controlled strain using devices that can mechanically induce tension or compression in a steady or time-dependent manner as necessary. These devices can also be fabricated to enable to local delivery of drugs.

[0044] Stresses may also be generated by external mechanical devices. In one embodiment, biodegradable sheets or meshes, coated with natural ECM molecules, are draped on the wound and stretched or compressed. The coating of bioadhesive molecules interacts with ligands on the cells within the wound directly, so that stretch or compression of the coated sheet with an external device is transduced selectively and directly to the cells without re-opening the wound.

[0045] In one embodiment, a stiff biodegradable wire can be coiled around a compliant biodegradable tube (with a diameter of about500 μm) coated with ECM proteins. Cells will be allowed to adhere to the surface. Upon subsequent inflation of the tube with fluid or air, the tube will protrude through the stiff coil, creating a local stretch of the adherent cells which is controlled by the degree of inflation. In a variation, a ECM protein-coated compliant tube can be positioned inside a stiff porous outer tube, such that on inflation, the inner tube protrudes through the pores of the outer tube, creating a local stretch. If the compliant tube is fabricated with

dialysis-membrane size pores, the inflation fluid can also be used to deliver drugs or, by adjusting protein content, to carry away edema fluid.

[0046] In one embodiment, stress application to cells may be accomplished using magnetic forces. Paramagnetic or ferromagnetic beads coated with integrin-ligands (e.g., RGD, integrin) may be applied directly to cells on the surface of a wound. Upon application of an external magnetic force, the cell surface-bound beads experience a pulling or twisting force which is transduced to the cytoskeleton and enhances signal transduction. For example, using, ferromagnetic beads, a torque force can be applied: first, a magnetizing pulse is applied, followed by a twisting field in a different direction for 5-15 min. The process can be repeated cyclically.

[0047] In another embodiment, elastomeric membranes may be constructed containing magnetic microbeads (e.g., less than 10 microns in diameter) distributed throughout the material of the membrane and the surface of the membrane is coated with molecules that mediate adhesion to ECM and cells. This wound dressing is applied directly to the surface of the wound and mechanical stresses are applied locally to adherent cells on the micron scale by applying constant or varying homogeneous magnetic fields of various intensity across the surface of the entire wound. Altering the size, distribution, and magnetic moment of the beads can vary the local stresses applied. This method can be combined with porous sheets to further concentrate stresses and strains within preferred micro-regions.

[0048] In one embodiment, stress may be generated by intrinsic cellular contraction. A compression resisting or self-expanding non-malleable material that can hold its shape in tension without the aid of an external device will allow cells "to pull against" and thereby generate isometric tension. One example is a metallic or polymeric mesh/matrix coated with bio-adhesive molecules and affixed to the wound in a compressed or stretched form, which then returns to its original shape upon release or other stimuli. The entire assembly can be biodegradable. The coated bio-adhesive molecules interact with ligands on cells within the wound such that stretching and compression is transduced to the cells directly. Feedback and regulability of forces can be described as follows.

[0049] Self-expanding material can be fabricated from shape-memory alloys, such as nitinol, which can change shape with thermal variations. Applied stress can be made time-dependent to correspond to the optimal rate of strain for wound healing. This can be accomplished by fabricating the material from a system of interconnected nitinol tubes, through which fluid of varying temperature can be circulated or by applying electrical current.

[0050] Polyethers such as poly(ethylene glycol) (PEG), poly(propylene glycol) (PPG), and poly(tetramethylene glycol) (PTMG) can be copolymerized with oligomers of D,L-lactic acid and terminated with acrylate groups to form photopolymerizable biodegradable macromers. Photopolymerizable hydrogels may also be similarly fabricated. Either the hydrogel or polymer form of the material can be injected as a fluid (mixed with ECM proteins for cell adhesion) into the wound and polymerized to various desired stiffnesses by varying exposure to light. Since the material is initially fluid, it will inherently conform to the shape of the wound and seal it. Air bubbles can be incorporated into the fluid for desired porosity. Stiffness can be maintained as the material biodegrades by renewed light exposure or injection of more material. Biodegradation will be most rapid on wound periphery and slower in the core, matching where the cells most need space or anchor. Hydrogels can be made to swell if desired, providing an active cell stretching element. Drug delivery can also be easily incorporated into either the hydrogel or the polymer.

[0051] Smart material composed of different intercalating meshes of material offer corresponding disparate resistances to biodegradation. This allows the material to maintain stiffness even as it is continuously degraded proportionally to the increase in wound cellularity. Such a device would prevent early dissipation of the resisting force in the device and guarantee long-lasting effect. Examples of such smart materials are described below.

[0052] The time-dependent viscoelastic properties of the polymeric or metallic mesh can be optimized to match its rate of strain under stress to the optimal rate of strain for cellular proliferation. For polymers and hydrogels, viscoeleastic properties can be modulated by varying the degree of cross-linking within the polymer, and/or by varying the interfibrillar material. The strain response can be made anisotropic as desired by combining multiple polymers within the material.

[0053] Pre-programming the response through a ratchet-like arrangement affixed to the wound can finely control viscoelasticity. The spacing between the ratchet teeth can be set to provide the desired time-dependent viscoelastic response that matches the optimal stimulus required for cellular proliferation. The ratchet mechanism can be powered internally using a stretched spring, or externally, by using a pneumatic device. The ratchet advancement can be controlled by sequentially biodegradable teeth (teeth made of materials that biodegrade at various kinetics), or by using a pneumatic device. Multiple ratchets can be stacked to achieve anisotropic responses.

[0054] Shear forces produce a strain on the surface cells of the wound distinct from absolute stretch, and can also be conducive to cell proliferation. Methods used to generate shear stress are inherently coupled to the ability to control pressure that imparts deep-layer strains in addition to surface-level shear. Shear is created in all cases by moving fluids, which can be used as a vehicle to deliver drugs, carry away wastes, and control edema, by varying protein content in the fluid. Depending on the shearing mechanism, the shear can be applied in a time-dependent fashion by varying, imposed flows, imposed pressures, or imposed surface translations. The magnitude of the shear is dependent, in all embodiments, on the viscocity and velocity of the circulating fluid and on the distance between the wound and the device.

[0055] It is still unclear whether it is laminar shear or turbulent that is most useful in wound healing. Closed-form analysis is provided for laminar shear and simplified geometries for which such analysis is straightforward. In general, turbulence can be achieved using each of the devices by enlarging the geometry or increasing the flow such that the Reynolds number exceeds 2,00. Analysis of turbulent flow is inherently empirical, and thus will not be provided here; however, it should be noted that the laminar stress on the wound can be used to compute an approximation of the magnitude of the turbulent stress.

[0056] Global shear stress may be applied to the surface cells of the wound using fluid circulation. The wound is covered with a conduit through which an external device applies fluid flow. An opening is made in the conduit at the site of the wound and sealed onto surrounding intact tissue, exposing the wound to the fluid. The velocity profile and the fluid viscosity control the shear stress. The external device and the shape of the conduit determine the velocity and pressure. Fluid viscosity can be varied as desired by modulating its PEG content. The fluid may also be used to deliver drugs, carry away wastes, and control edema. To induce turbulence, the geometry and fluid velocity must be such that the Reynolds Number is greater than 2500. This method may be particularly useful for modulating the growth and viability of engineered tissues in vitro.

[0057] For steady, laminar flow Q provided by an external pump, and plane plastic sheet covering the wound at a distance H, the velocity profile is

$$u(y)=\frac{3Q}{4H}\left(1-\left(\frac{y}{H}\right)^2\right).$$

Given fluid viscosity$v$, the shear stress on the wound is

$$\tau_{yx}(y=H)=-\frac{3\mu Q}{2H^2}.$$

The fluid viscosity can be time-dependent. Given a reference pressure p_0, the pressure distribution is

$$p(x) = p_0 - \frac{3\mu Q}{2H^3}x.$$

[0058] For an imposed pulsatile pressure gradient $G = G_0(1+\varepsilon \sin \omega t)$ with fluid kinematic viscosity ν, and a cylindrical tube of radius R such that the Womersley number

$$\Re = \frac{R^2/\nu}{\omega^{-1}} << 1,$$

the velocity profile beyond start-up time is

$$\frac{u}{G_o R^2/\nu} = \frac{1}{4}\left(1-\left(\frac{r}{R}\right)^2\right)(1+\sin \omega t) + \Re \frac{\cos \omega t}{64}\left(4\left(\frac{r}{R}\right)^2 - \left(\frac{r}{R}\right)^4 - 3\right) + O(\Re^2)$$

[0059] This corresponds to a relatively viscous fluid, with pressure oscillating at a relatively low frequency, in a small cylindrical tube. The shear stress on the wound is

$$\tau_{rz} = \rho G R\left(\frac{\Re \cos \omega t}{16} - \frac{1+\sin \omega t}{2}\right)$$

given fluid density ρ. The pressure distribution is $p(z) = p_0 - G_0 z(1+\varepsilon \sin \omega t)$ and is referenced to pressure p_0.

[0060] Shear stress can also be created by forcing fluid through thin slots or pinholes within a plate placed close to the wound. This system allows the site-specific control of shear stress within the wound, as areas of the wound adjacent to the thin slots will experience significantly higher shear stress than areas further away. High shear stress may created with very low fluid flow. Site-specific control may be useful in instances of uneven healing, when unhealed areas of the wound may need more stimulus than the healed areas. As with the external circulation system, the fluid viscosity can be varied as desired by increasing or decreasing its PEG content, and can be also used to deliver drugs, carry away wastes, and control edema by its osmolarity. To induce turbulence, the geometry and fluid velocity must be such that the Reynolds number is greater than 2,500.

[0061] An analysis of the single pinhole system, providing point-specific shear stress with laminar flow will be presented here as an illustration. For fluid injected with flow $2Q$ into a hole radius $R0$ at center of a disk of radius R located a distance $2H$ above the wound, the velocity profile is

$$u_r = \frac{3Q}{4\pi rH}\left(1-\left(\frac{z}{H}\right)^2\right)$$

assuming that the gap is thin ($H/R << 1$) and the injection hole is small ($R0/R << 1$). Given fluid viscosity m, the resulting shear stress is

$$\tau_{rz} = -\frac{3\mu Q}{2\pi rH^2}$$

with r the distance from the pinhole. The $1/r$ dependence demonstrates the possibility of creating high shear stress locally with low flows. The resulting pressure distribution is also dependent on distance from the pinhole, and is

$$p = p_0 - \frac{3\mu Q}{2\pi H^3}\ln r$$

when referenced to pressure p_0.

[0062] Figure 9 depicts a clinical application of another embodiment according to the invention. This embodiment adds an in-flow system for the delivery of fluids, and an outflow system for the removal of fluids and the application of a vacuum to the wound for integration with a biodegradable matrix 105 the overlying non-degradable sponge 110 such as polyurethane, and the occlusive dressing 115. The biodegradable matrix has been described. A polyurethane or polyvinyl alcohol sponge designed to provide both an air-tight seal for the system and to protect the wound 100 from infection. This embodiment allows unidirectional transport of fluids 130 and cell delivery 135 parallel to the surface of the wound 100. One end of the wound 100 has a distributed network of tubing that allows uniform application of fluid on one end of the wound through an inlet manifold 145. The other end of the wound has a distributed tubing network allowing for the egress of fluid through an egress manifold 150 via vacuum, pressure or siphon drainage. This fluid parallel to the surface applies a shear force to the wound 100 stimulating the wound cells to proliferate, and allowing transport of growth factors, oxygen, nutrients, antimicrobials and cells to the wound site. Egress of fluid allows for transport of waste products including carbon dioxide, bacteria, cytokines and nitrogenous breakdown products. In other embodiments. In a further embodiment, fluid collected in the egress manifold 150 is directed through a micropore 150 filter via the network tubing 140 and returned to the inlet manifold 145 by a prime moving source such as roller pump 160.

[0063] In another embodiment, a roller system may be employed to effect parallel translation. The translation of a surface parallel to the wound imparts motion to fluid in the gap between the translating surface and the wound, resulting in shear stress. For certain gap dimensions,

tremendous positive pressure can be generated within the gap. This pressure, which can also be used to stretch cells and control edema, can be set as desired by varying the shape of the gap and the viscosity of the fluid. For fast enough translation, the motion of *air* in the gap may be enough to create adequate shear stress. To induce turbulence, the geometry and fluid velocity must be such that the Reynolds number is greater than 2500.

[0064] As an example, continuous parallel translation can be accomplished with a roller device, essentially a miniaturized version of the supermarket conveyor belt. Rollers with surfaces that can adapt to the contour of the wound can also be made through the use of a compliant material (thick rubber) which can be padded with sponge foam or built with multiple encased springs.

[0065] Under laminar flow conditions, for a thin fluid-filled gap $h(x)$ between the wound and the roller surface of length L ($h/L << 1$), and translation velocity $U(t)$, the velocity profile is

$$u(y)=U\left(1-\frac{y}{h(x)}\right)+\frac{1}{6h^3(x)}\left(\frac{Uh(x)}{2}-\frac{6\mu U}{L}\int_0^L\frac{dx}{h^2(x)}\right)\left(y^2-yh(x)\right)$$

[0066] The integral can be evaluated numerically depending on the particular shape of the roller $h(x)$. The resulting shear stress on the wound, given a fluid viscosity of μ is

$$\tau_{yx}=\frac{\mu U}{h(x)}\left[\frac{11}{12}-\frac{\mu}{Lh(x)}\int_0^L\frac{dx}{h^2(x)}\right]$$

[0067] The pressure distribution, referenced to a pressure p_0 is

$$p(x)=p_0-\int_0^x\frac{12\mu}{h^3(x)}\left(\frac{Uh(x)}{2}-\frac{6\mu U}{L}\int_0^L\frac{dx}{h^2(x)}\right)dx$$

[0068] The gap shape $h(x)$, translation velocity $U(t)$, and fluid viscosity μ can be adjusted as necessary to achieve both the desired shear stress and pressure distribution profile.

[0069] In one embodiment, perpendicular and multicomponent translation of a surface in a direction perpendicular to the wound imparts motion to fluid in the gap between the translating surface and the wound, resulting in radial motion and shear stress. For certain gap dimensions, large pressures can be generated within the gap. To induce turbulence, the geometry and fluid velocity must be such that the Reynolds number is greater than 2,500.

[0070] As an example, the oscillating perpendicular motion of a disk or a piston in an enclosed volume can force fluid within that volume to translate radially, with uniform time-dependent pressure throughout the wound. y combination of perpendicular, parallel, or rotational translation can also be used to create the appropriate shear stress, as desired.

[0071] For a flat plate at a distance $h(t)$ from the wound moving with vertical velocity $U(t)$, under laminar flow conditions, the radial velocity is

$$u_r = \frac{3}{8}U\left(\frac{r}{h}\right)\left(1-\left(\frac{z}{h}\right)^2\right),$$

and the vertical velocity is

$$u_z = -\frac{3}{2}U\left(\frac{z}{h}-\frac{1}{3}\left(\frac{z}{h}\right)^3\right).$$

Given a fluid viscosity μ, the shear stress is

$$\tau_{zr} = \frac{3\mu Ur}{4h^2},$$

increasing away from the center of the plate. Given reference pressure p_0, the pressure distribution is

$$p = p_0 - \frac{3}{8}\frac{\mu UR^2}{h^3}\left(1-\left(\frac{r}{R}\right)^2\right).$$

The velocity distribution, shear stress, and pressure can all be time-dependent.

[0072] The generation of shear in a two-dimensional plane as previously described can be extended to a three-dimensional volume for severe wounds that form cavities. In this instance, a moving surface is inserted into the cavity, surrounded with fluid, and continuous motion is provided to generate the appropriate shear stress. Fluid viscosity and protein content can be adjusted to regulate shear stress and edema, and drugs can be delivered through the fluid. To induce turbulence, the geometry and fluid velocity must be such that the Reynolds Number is greater than 2,500.

[0073] As an illustration, a caged ball, inserted into the wound cavity, can be continuously rotated to generate the necessary stress in a cavity. The entire system can be made of biodegradable polymers, so that an additional operation will not be needed to retrieve the device after the wound has healed.

[0074] Starling forces dictate the fluid pressure balance in the wound milieu. The fluid transfer rate (J) across a membrane is given by $J = RS[(P_C - P_{IF}) - (\pi_C - \pi_{IF})]$ where R is the hydraulic conductance of the membrane, S is the surface area, P is hydrostatic pressure and π is the oncotic pressure in the cell (subscript C) and in the interstitial space (subscript IF). This relationship can be used to control wound edema, and also to induce cell strain.

[0075] Loss of endothelial integrity causes large proteins such as albumin to leak into the wound space, raising the interstitial oncotic pressure. Fluid consequently flows into the interstitial space, resulting in wound swelling (edema). Such edema can be minimized using our devices through the control of either hydrostatic pressure or oncotic pressure. The hydrostatic pressure can be controlled directly either by altering the pressure profile in the fluid flow devices (such as by changing flow conduit geometry or flow velocity), or through the mechanical application of pressure (such as with a vacuum or high pressure cell). Oncotic pressure might be controlled mechanically (such as by changing flow to alter protein washout and content), or through the actual delivery of oncotic proteins (such as albumin) within the flow.

[0076] Cells will swell or shrink depending on the net pressure drop across its membrane. The net effective pressure drop is essentially the difference between the hydrostatic pressure drop and the oncotic pressure drop across the cell membrane. By controlling these pressures, potentially in a time-dependent manner, it is thus possible to induce the cells to swell or shrink, thereby causing the appropriate cell strain. Pressures can be manipulated, as in the control of edema, by influencing both hydrostatic and oncotic pressures. The hydrostatic pressure can be controlled by altering the pressure profile in the fluid flow devices (such as by changing flow conduit geometry or flow velocity), or through mechanical application of pressure (such as with a vacuum or high pressure cell). Oncotic pressure might be controlled mechanically (such as by changing flow to alter protein washout and content), or through the actual delivery of oncotic proteins (such as albumin) within the flow.

[0077] Differences in surface energy between biomaterials and the wound can cause direct stresses and deformation on wounds. This is most easily appreciated in the common experiment demonstrating capillary action. Small porosity channels can induce specific forces on the wound resulting in cellular deformation. A device that used multiple small tubes oriented perpendicular to the wound would induce MicMFs on the wound. In alternative embodiments, a membrane with an array of different adjacent surface energies could result in micromechanical deformations of the wound.

[0078] Surface tension interactions at the wound surface can induce convolutions in the wound surface without the use of suction or vacuum. In this invention, porous materials are made of a small pore size 10 to 500 μm pores that induce forces on the wound through capillary action. The capillary pressure can be further increased by coating the matrices with bioactive molecules that bind to specific cell receptors such as fibronectin, Integrins, laminin and fibrin. This will allow a sponge to be produce that will apply micromechanical forces to the cells at the

wound surface without the use of a vacuum. Control of the surface energy can be obtained by the density of the bioactive molecules placed on the surface of the matrix and on the porosity characteristics of the matrix.

[0079] Biomaterials will be critical to the function of these devices, as they must be non-toxic, non-immunogenic, and non-inflammatory while maintaining their structural characteristics. Several permanent biomaterials including polypropylene, polyethylene, Nylon, stainless steel, titanium, carbon, and silicone may be useful. In addition, biodegradable materials that interact with the wound in a predictable fashion may also be practicable; these include collagen, glycosaminoglycan, polylactic and polygalactic acid polymers, polydioxanone polyglyconate, and polyglecaprone. One important property of biomaterials is their pore structure; pores greater than 10 μm allow for vascular in-growth. For degradable polymers, the rate of degradation can be quantified based on tissue type and wound location. Changing the cross-link density, copolymerization, orientation and the degree of crystalinity of the polymer can control this degradation.

[0080] The sheet material can be fabricated from, or coated with, one or a combination of polymers to deliver drug. Examples of biocompatible polymers include, but are not limited to, ethylene-vinyl acetate copolymer (EVAc), Poly-L-Lactic Acid (PLLA), alginate-heparin-sepharose, polyacrylic acid hydrogels, polyurethane, and polyurethane-polythelene oxide copolymers. The polymer can be made of one or a combination of biodegradable materials, such as, but not limited to, PLLA, polyglycolic acid, polycaprolactone, polyorthoesters, or fibrin matrices, all of which can incorporate drug for controlled release. Cross-linked gels of natural biomolecules, such as collagen or fibrin, or composed of synthetic peptides, nucleic acids, or carbohydrates, also may be utilized for this application.

[0081] In one embodiment, a feedback control system employing biosensors may be utilized for optimizing the rate of wound healing. Depending on the particular wound type, optimal strains and rates of strains can be time-dependent, or even dependent on the state of healing. Therefore, to use the system described in this disclosure to deliver optimal MicMF, a suitable mechanism must be designed to obtain data on the degree or lack of healing occurring in the wound. As described above, "smart" self-adjusting polymers represents a method for adapting force generation automatically to the state of wound healing. In addition to such implicit feedback regulation, a model of the invention is the use of an explicit feedback system in which biological parameters are measured and used to control the force generation or drug delivery. Biological or physical markers of wound healing can be used to detect such changes. Examples

of such markers include either changes that are directly responsible for wound healing such as cellular proliferation, rate of neovascularization, or changes that are correlated with wound healing. For instance, a wound may become drier as it heals, its color may change, the level of the wound may rise, the compliance of the wound may increase, or any of these and other events may occur in combination to give an indication of wound development process. Alternately a lack of any of these markers may signal that the device is producing either a too high or a too low an output. For instance, if stretch rate is used to obtain wound healing, a greater or less than optimal rate for the wound in question may not produce the desired results.

[0082] Sensor mechanisms that take advantage of the above markers might include a piezoelectric strain gauge mounted on the wound, a mechanical or optical device that measures the rising of the wound, an optical device that can detect color changes or hemoglobin levels (due to new vessel growth) in the wound, or other devices that can measure these changes. These sensors would input data into the expert control system that might output a change in the stretch rate, a change in the shear rate, a change in pressure, etc. These sensors can also direct a change in the level of drug delivery given to the wound. Figure 7 presents a schema in which inputs to the sensor system are modified by the sensor based on the error it sees between the progress of wound healing and an optimal target parameter set.

[0083] As shown in Figure 10A, another embodiment of the invention may include a wound sensor array 170. The sensor array 170 is a multi-sensor designed to monitor the microenvironment of the wound bed 100. The parameters measured include wound temperature, pH, perfusion, pO2, pCO2, and glucose. The multisensor 170 can be placed through the biodegradable matrix 105 into the wound 100 itself to a depth of 1 to 3 mm. The sensor 170 array can be placed at any point in the wound 100 and multiple sensor probes 175 can be used to monitor the wound 100 at different points. As shown in Figure 10B and in one embodiment, the sensor array 170 may comprise a linear arrangement. Alternatively, the size and configurationof the sensor array may adapted for a specific wound and tissue type. The disparate sensor probes 175 are entrained in the matrix 105 and fed through the occlusive dressing 115 to a sensor output 180. This sensor output 180 provides valuable information about the wound microenvironment that can lead to changes in managing the patient.

[0084] A finite element model can predict optimal pore design of non-degradable materials such as polyurethane. The wound can be modeled as an isotropic linearly elastic tissue in two dimensions with a fine mesh applied. Applying micromechanical forces to the wounds so that the surface is stretched by 5 to 20 percent will induce cellular division and application of

cytokines. The finite element model allows calculation of optimal force application to a variety of biological tissues that can be characterized by their stiffness or Young's modulus of elasticity. Some tissues such as mucosa and fat are very pliable, others such as dermis and fascia stiffer, and tissues such as cartilage and bone quite stiff. The finite element model allows optimal design of pore structure and optimization of applied sub-atmospheric pressure based on the stiffness of the wound tissue. (see diagrams at the end of the provisional patent).

[0085] All biomaterial surfaces can be modified by ionic, covalent, hydrogen or mechanical bonds of surface active agents, or polymers. In addition bioactive agents including antibiotics, RGD peptides, collagen, anticoagulants, heparin, glycosaminoglycans, and electrically or magnetically charged particles can be added to the device surface.

[0086] Addition of cells to the micromechanical devices will allow for production of soluble growth factors as well as additional cells to the wound. A method to seed cells within a collagen-GAG matrix to cause a functional restoration of the epidermis in a full-thickness wound. Studies have shown that lethally irradiated neonatal fibroblasts seeded onto a Nylon-collagen matrix increase the healing of partial thickness burns. The cells can be genetically engineered to secrete essential growth factors such as bFGF, EGF or KGF.

[0087] Devices designed to apply MicMFs to the wound are ideally suited as drug delivery devices. Drugs useful in the treatment of wounds include antibiotics: silver, silver nitrate, mafenide acetate, povodine iodine, silver sulfadiazene, macrolides, penicillins, cephalosporins, aminoglycocides and quinolones. Other drugs of use in wound healing include soluble growth factors, angiogenic factors, vitamins, peptides and genetic material. Incorporation of these drugs into the polymer construct of the device can be designed for controlled release over time.

[0088] Some embodiments of the invention can be made to be entirely automated, self-contained, and portable. For example, the entire roller-system or oscillating flat plate or forced injection assemblies can be built, together with feedback and controller systems, into a closed battery-powered unit that the patient can wear on top of the wound, thus allowing ambulation. Translation velocities and oscillation frequencies can be pre-programmed, or continuously adapted according the built-in biological expert system in the feedback and controller system. Drug delivery can similarly be injected into the moving fluid at pre-programmed times and continuously monitored by the feedback and controller system.

[0089] The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. Therefore, it must be expressly understood that the foregoing embodiments are therefore to be considered in all respects illustrative rather than

limiting on the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

CLAIMS

1. A therapeutic device for promoting tissue growth, said device comprising:

a variable composition matrix for application to the tissue, said matrix having a plurality of pores;

a means for establishing a pressure differential between said matrix and the surrounding environment; and

a means for delivering micro-mechanical forces to the tissue through said matrix.

2. The device according to claim 1, wherein said pores have a diameter from about 1 μm to about 10,000 μm.

3. The device according to claim 1, wherein said pores have a diameter from about 50 μm to about 1,500 μm.

4. The device according to claim 1, wherein said pores have a diameter from about 20 μm to about 2,000 μm.

5. The device according to claim 1, wherein said matrix is a non-biodegradable material.

6. The device according to claim 1, wherein said matrix comprises at least a first layer adjacent to the tissue and a second layer adjacent to said first layer.

7. The device according to claim 6, wherein said first layer is a porous biodegradable material and said second layer is a nondegradable sponge, said first layer is adapted for integration with the tissue.

8. The device according to claim 1, wherein said matrix is formed from micro-fabrication techniques.

9. The device according to claim 8, wherein the diameter and shape of said pores of said matrix are optimized for local targeted concentration of the micro-mechanical forces to the tissues.

10. The device according to claim 1, wherein the matrix is a collagen, elastin, fibornectin, or laminin.

11. The device according to claim 1, wherein the matrix is a polyglycolic or polylactic acid.

12. The device according to claim 1, wherein the matrix is coated with at least one of extracellular matrix factors, peptide fragments, synthetic molecules, and growth factors.

13. The device according to claim 1, wherein the matrix is coated with exogenous growth factors and cytokines.

14. The device according to claim 1, wherein said means for delivery of micro-mechanical forces is adapted for continuous operation.

15. The device according to claim 1, wherein said means for delivery of micro-mechanical forces is adapted for time-cycled operation.

16. A therapeutic device for promoting tissue growth, said device comprising:

a variable composition matrix for application to the tissue, said matrix having a plurality of pores;

a substantially compliant biodegradable tube wherein said tube is coated with ECM proteins and configured for inflation;

a substantially stiff biodegradable wire, wherein said wire is substantially coiled about said tube; and

a means for inflating said tube so as to exert micro-mechanical forces on the tissue.

17. The device according to claim 2, wherein said tube comprises a plurality of dialysis-membrane sized pores.

18. A therapeutic device for promoting tissue growth, said device comprising:

a variable composition matrix for application to the tissue, said matrix having a plurality of pores;

a plurality of magnetic microbeads;

a means for applying a magnetic field to said magnetic microbeads so as to exert micro-mechanical forces on the tissue.

19. The device according to claim 18, wherein said magnetic microbeads further comprise a coating of integrin-ligands.

20. The device according to claim 18, further comprising an elastomeric membrane, wherein said magnetic microbeads are embedded in said membrane.

21. The device according to claim 1, further comprising a sensor array for monitoring the microenvironment of a wound bed of a patient, said sensor array monitoring at least one biologic wound parameter for patient management.

22. The sensor array according to claim 21 wherein at least one of wound temperature, wound perfusion, wound pH, wound pO_2, wound pCO_2, and wound glucose is measured.

23. The device according to claim 21, further comprising a self-adaptive matrix material and feedback control.

24. The sensor array according to claim 22, wherein the sensor comprises a piezoelectric gauge.

25. The sensor array according to claim 22, wherein the sensor comprises an optical device.

26. The sensor array according to claim 22, wherein the sensor is sized and configured for patient ambulation.

27. A therapeutic system for treating a wound, said system comprising:

a biodegradable matrix for direct application of micro-mechanical forces to the wound;

a non-degradable sponge overlying said biodegradable matrix;

an occlusive dressing overlying said sponge and sealing the wound from the surrounding environment; and

a pump means in fluidic communication with the therapeutic system for imposing a pressure gradient upon the wound.

28. The system according to claim 27, further comprising a means for delivery of fluids to said biodegradable matrix and a means for removal of fluids from said biodegradable matrix.

29. The system according to claim 28, further comprising a fluid recirculation system having a filtration device and recirculation pump.

30. The therapeutic system according to claim 4, wherein said system further comprises a non-degradable material having a plurality of pores, said pores dimensioned and configured according to a mathematical modeling method for a given biologic tissue.

31. The system of claim 6, wherein the mathematical modeling method is finite element analysis.

32. The therapeutic system according to claim 27, wherein said system further comprises a matrix material for direct application to the wound, said matrix material having a plurality of pores sized and configured for inducing micro-mechanical force to the wound through capillary action.

33. The system according to claim 32, wherein said pores have a diameter from about 10 μm to about 500 μm.

34. The system according to claim 32, wherein the material is coated with bioactive molecules selected from the group consisting of fibronectin, integrins, laminin and fibrin.

35. The system according to claim 34, wherein the surface energy is modulated by the density of the bioactive molecules.

36. The system according to claim 35, wherein the surface energy is further modulated by the size of said pores.

37. A therapeutic system for the treatment of wounds in a mammal, said system comprising:

a biodegradable matrix applied to the wound bed, said matrix having a plurality of pores with a diameter of about 50 μm;

a nondegradable sponge applied to said biodegradable matrix;

an occlusive dressing adhesively attached to said nondegradable sponge;

a pump means for establishing a pressure differential between the wound bed and the ambient environment; and

a connective means having first and second ends, said connective means attached at the first end to said pump means and attached at the second end to said occlusive dressing.

38. A method for promoting tissue growth, said method comprising the steps of:

a. providing a variable composition matrix being at least partially biodegradable and having a plurality of pores;

b. applying said matrix adjacent to the tissue;

c. establishing a pressure differential between said matrix and the ambient environment; and

d. delivering micro-mechanical forces to the tissue through said variable composition matrix.

39. The method of according to claim 38, wherein said pores have a diameter from about 1 um to about 10,000 um.

40. The method according to claim 38, wherein said pores have a diameter from about 50 μm to about 1500 μm.

41. The method according to claim 38, wherein said pores have a diameter from about 20 μm to about 2000 μm.

42. The method according to claim 38, wherein said matrix comprises at least a first layer and a second layer.

43. The method according to claim 38, wherein the first layer is a porous biodegradable material and the second layer is a nondegradable sponge, the first layer integrating with wound tissue ingrowth.

44. The method according to claim 38, wherein said matrix is formed using microfabrication techniques.

45. The method according to claim 38, wherein the diameter and shape of said pores of said matrix are optimized for local concentration of the micro-mechanical forces to the tissues.

46. The method according to claim 38, wherein the matrix is a collagen, elastin, fibornectin, or laminin.

47. The method according to claim 38, wherein the matrix is a polyglycolic or polylactic acid.

48. The method according to claim 38, wherein the matrix is coated with at least one of extracellular matrix factors, peptide fragments, synthetic molecules, and growth factors.

49. The method according to claim 38, wherein the matrix is coated with exogenous growth factors and cytokines.

50. The method according to claim 38, wherein said micro-mechanical forces are applied continuously.

51. The method according to claim 38, wherein said micro-mechanical forces are cycled over time.

52. The method according to claim 38, further comprising the step of monitoring the microenvironment of a wound bed of a patient.

53. The method according to claim 52, wherein at least one of wound temperature, wound perfusion, wound pH, wound pO_2, wound pCO_2, and wound glucose is monitored.

54. The method according to claim 52, further comprising a self-adaptive matrix material and feedback control.

55. The method according to claim 52, wherein the sensor comprises a piezoelectric gauge.

56. The method according to claim 52, wherein the sensor comprises an optical device.

57. The method according to claim 52, wherein the sensor is sized and configured for ambulation of a patient.

58. A method for treating a wound of a mammal, said method comprising the steps of:

a. applying a biodegradable matrix to the wound, said matrix having a plurality of pores;

b. adhering a non-degradable sponge overlying said biodegradable matrix;

c. positioning an occlusive dressing overlying said sponge and sealing the wound from the surrounding environment; and

d. delivering micro-mechanical forces to the tissue through said matrix.

59. The method according to claim 58, further comprising the step of imposing a pressure differential between said matrix and the surrounding environment.

60. The method according to claim 58, further comprising the steps of (a) delivering fluids to a first end of said biodegradable matrix and (b) removing fluids from a second end of said biodegradable matrix.

61. The method according to claim 60, further comprising the steps of (a) filtering the fluid from a second end of said biological matrix and (b) recirculating the fluid to a first end of said biological matrix.

62. The method according to claim 58, said matrix comprising a non-degradable material having a plurality of pores, said pores dimensioned and configured according to a mathematical model technique for a given biologic tissue.

63. The method according to claim 58, wherein the mathematical modeling method is finite element analysis.

64. The method according to claim 58, wherein step d) is performed through capillary action.

65. The method according to claim 64, wherein said pores have a diameter from about 10 μm to about 500 μm.

66. The method according to claim 64, wherein said matrix material is coated with bioactive molecules selected from the group consisting of fibronectin, integrins, laminin and fibrin.

67. The method according to claim 64, wherein the desired surface energy is modulated by the density of the bioactive molecules.

68. The method according to claim 64, wherein the desired surface energy is further modulated by the size of said pores.

69. A method for treating a wound of a mammal, said method comprising the steps of:

a. applying a biodegradable matrix to the wound, said matrix having a plurality of pores with a diameter of about 50 μm;

b. adhering a nondegradable sponge to said biodegradable matrix;

c. adhesively attaching an occlusive dressing to said nondegradable sponge; and

d. exerting a pressure differential between said matrix and the surrounding environment for delivery of micro-mechanical forces to the wound.

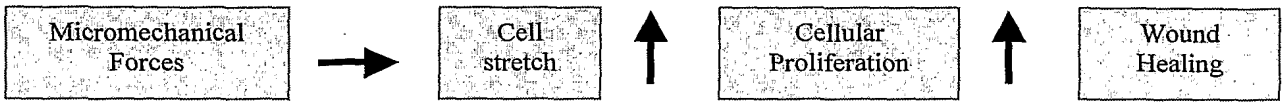
Micromechanical Forces
Cell stretch
Cellular Proliferation
Wound Healing

FIG. 1

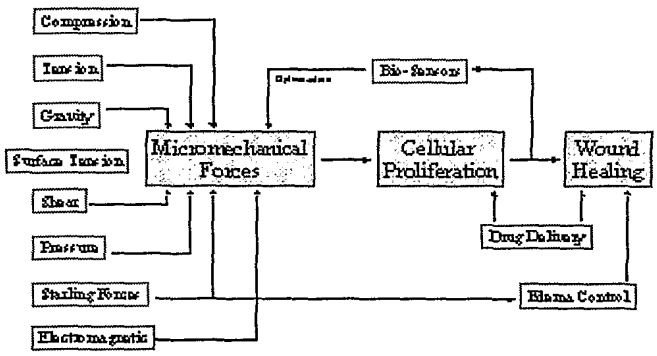
Compression
Tension
Gravity
Surface Tension
Shear
Pressure
Starling Forces
Electromagnetic
Micromechanical Forces
Bio-Sensors
Cellular Proliferation
Wound Healing
Drug Delivery
Plasma Control

FIG. 4

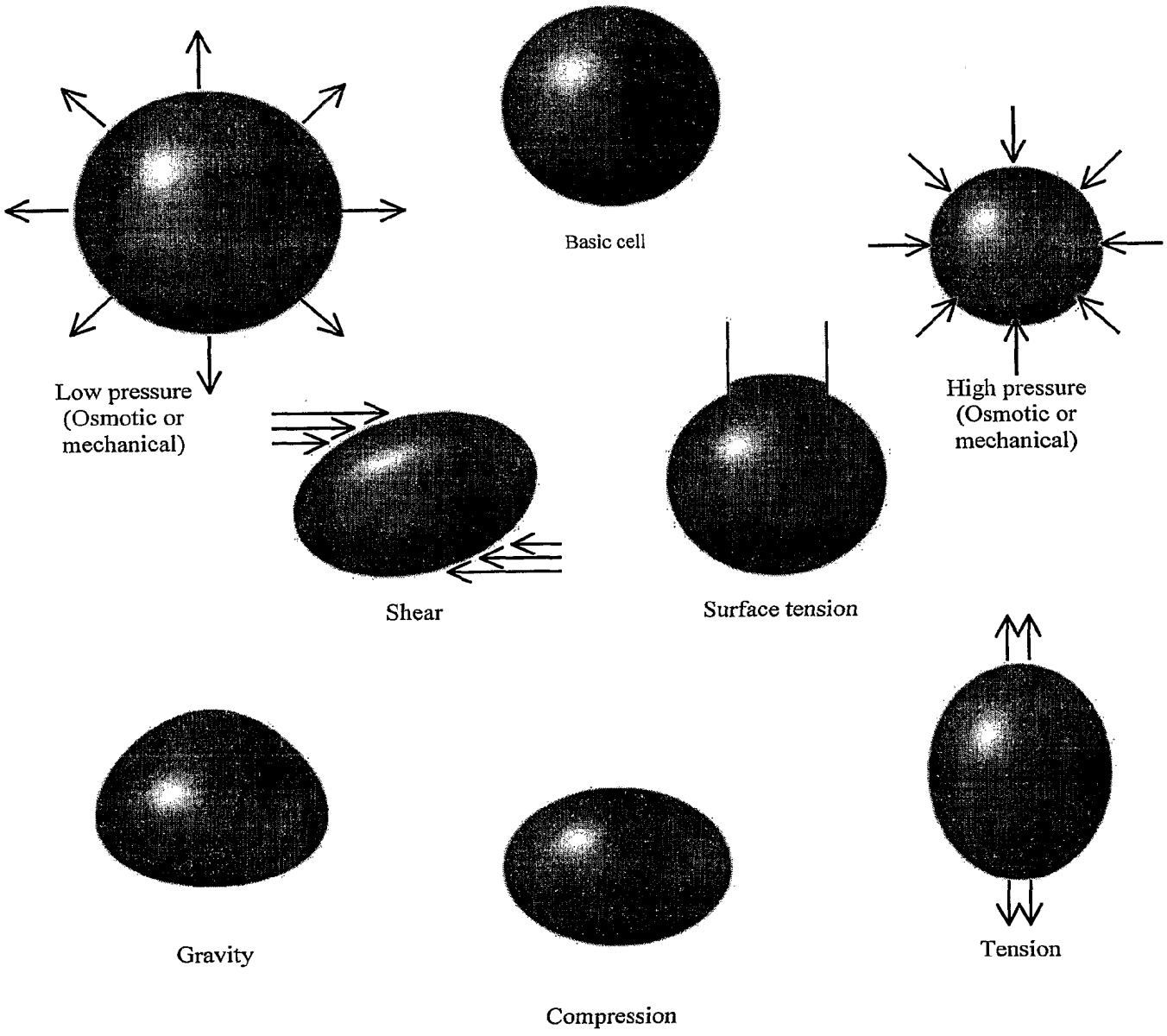
Basic cell
Low pressure
(Osmotic or
mechanical)
High pressure
(Osmotic or
mechanical)
Shear
Surface tension
Gravity
Compression
Tension

FIG. 2

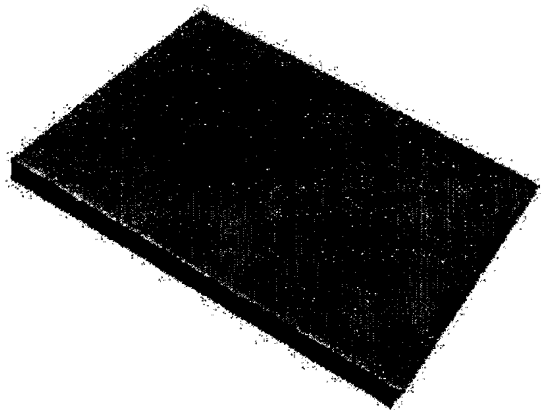

FIG. 3A

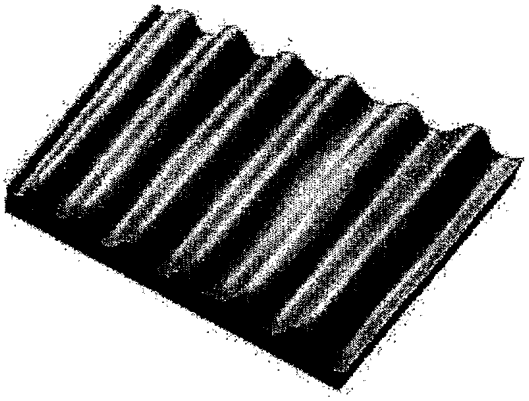

FIG. 3B

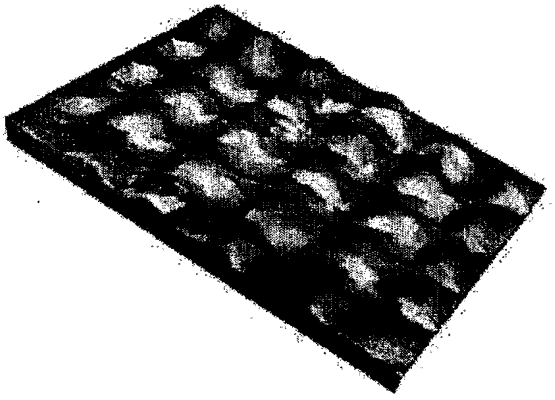

FIG. 3C

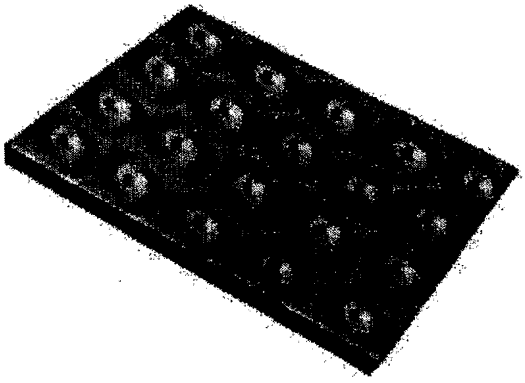

FIG. 3D

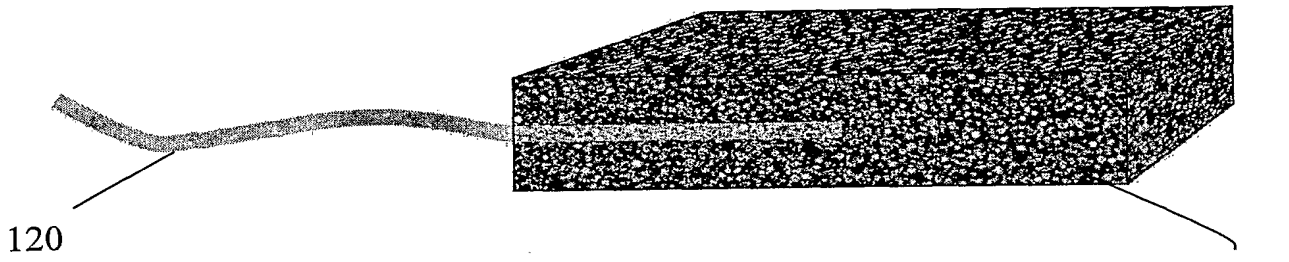
120
105

FIG. 5

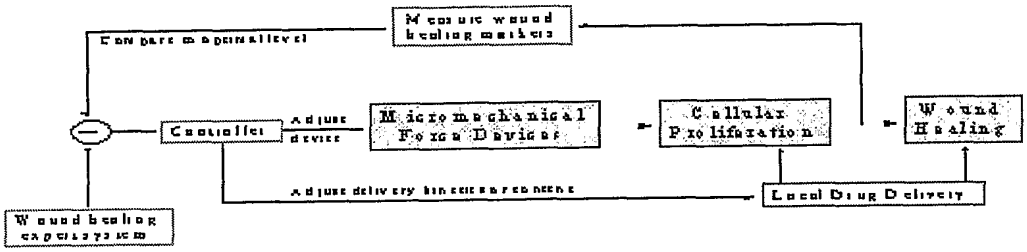
Micromechanical Force Devices
Cellular Proliferation
Wound Healing
Local Drug Delivery

FIG. 7

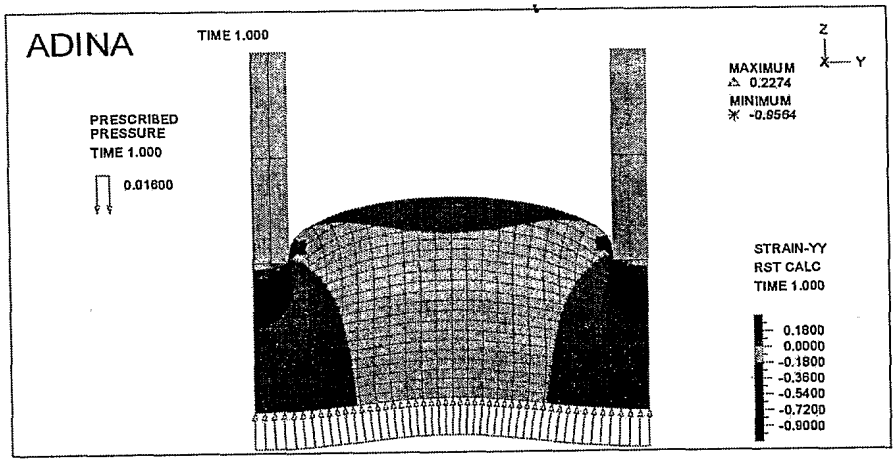

FIG. 6A

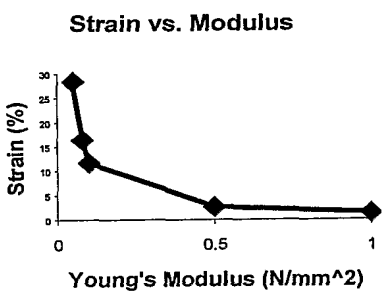

FIG. 6B

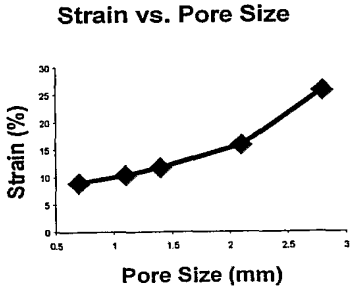

FIG. 6C

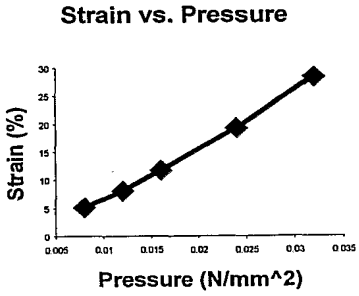

FIG. 6D

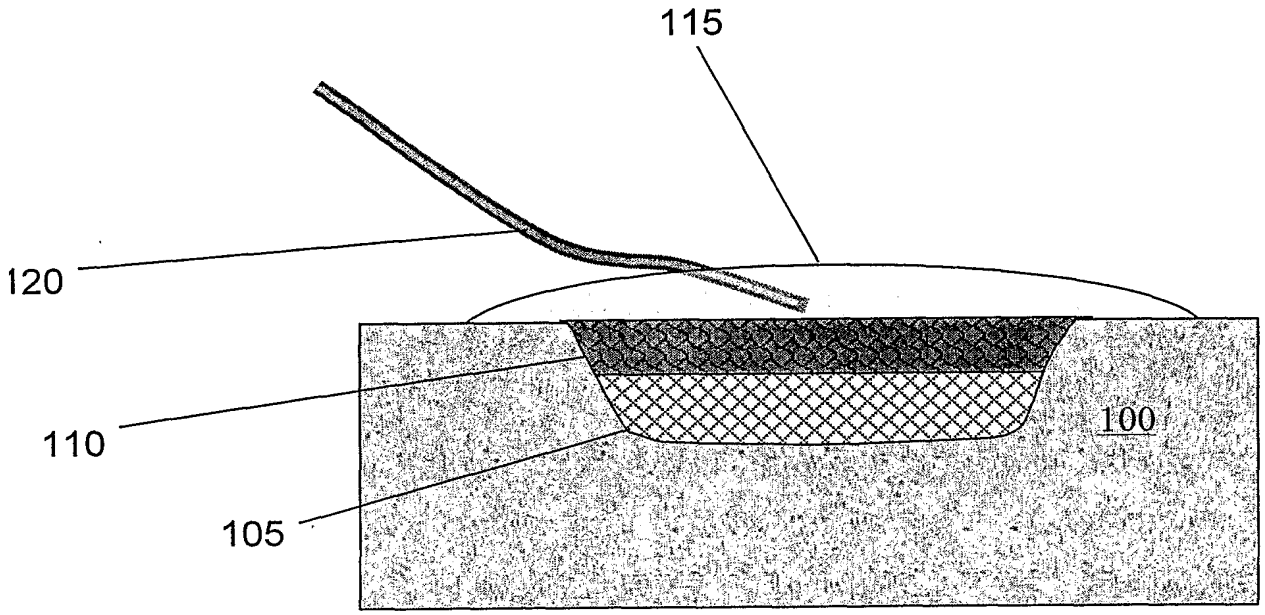

FIG. 8A

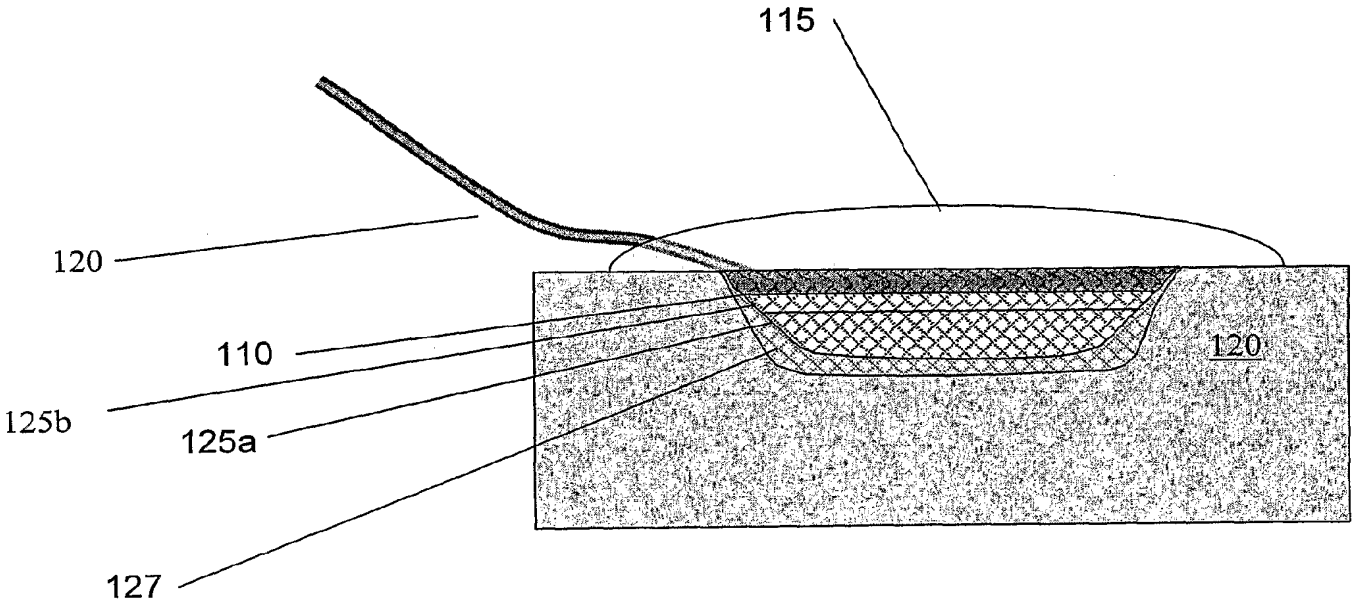

FIG. 8B

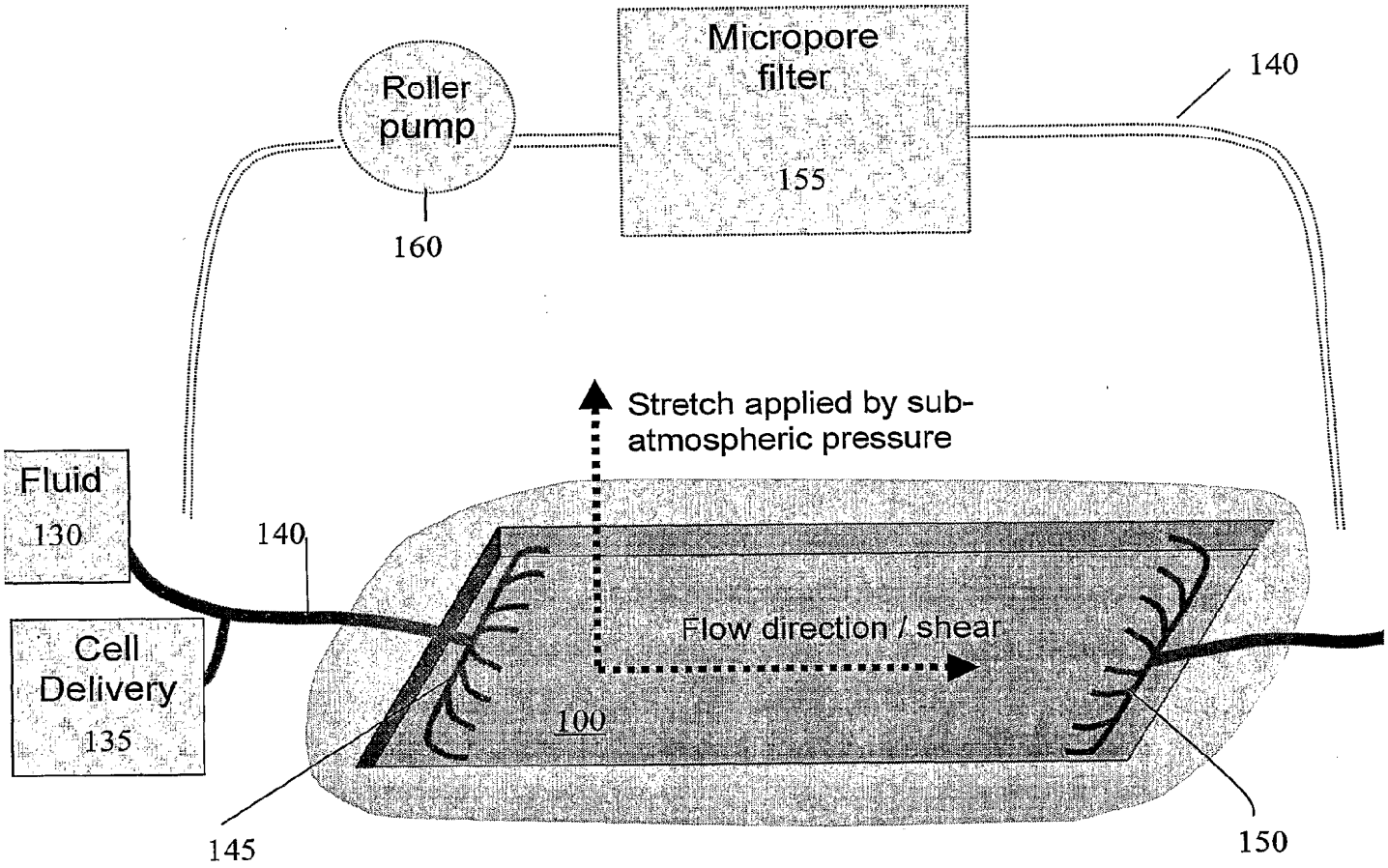
Micropore filter
155
Roller pump
160
140
Stretch applied by sub-atmospheric pressure
Fluid
130
140
Cell Delivery
135
Flow direction / shear
100
145
150

FIG. 9

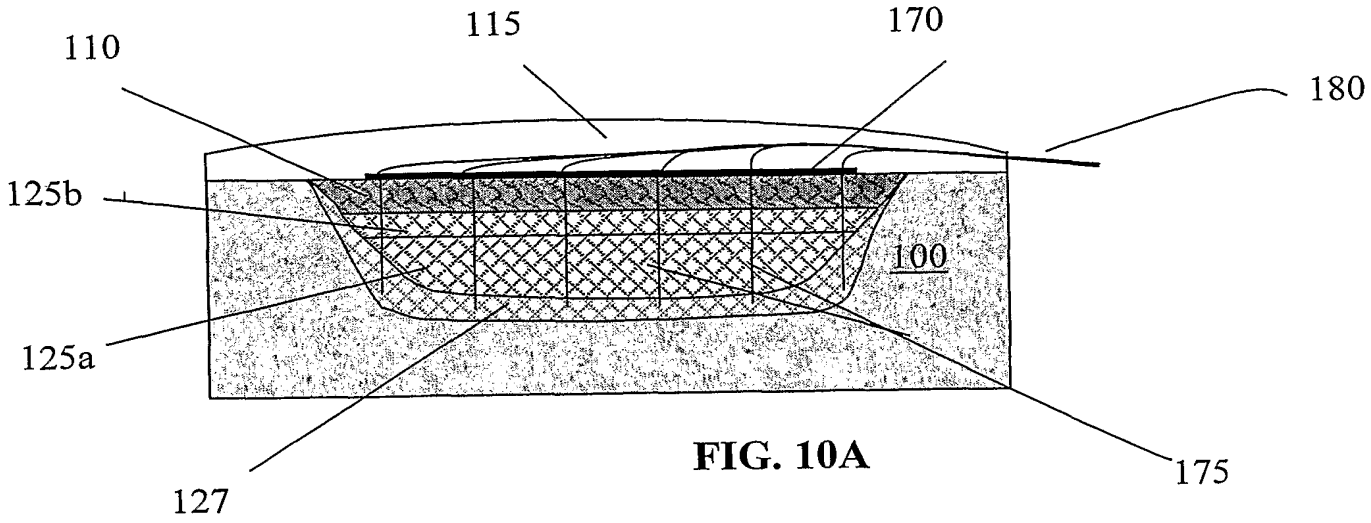

FIG. 10A

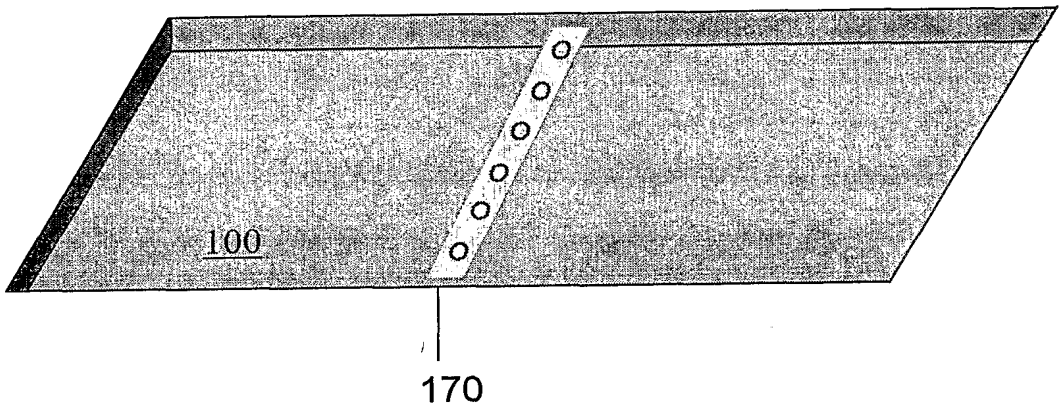

FIG. 10B

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— *of inventorship (Rule 4.17(iv)) for US only*

Published:
— *without international search report and to be republished upon receipt of that report*

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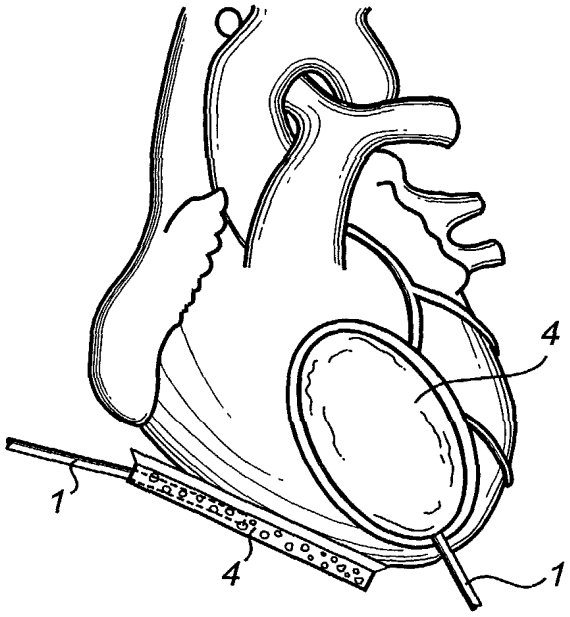
(54) Title: A METHOD, A DEVICE, AND A SYSTEM FOR ORGAN RECONDITIONING AND A DEVICE FOR PRESERVING AN INTERNAL BODYORGAN



(57) Abstract: A device for reconditioning an internal bodyorgan having or risking a functional failure or impairment associated with a fluid collection therein comprises a tube having a proximal end adapted for connection to a vacuum source, and a distal end portion having a plurality of openings. A chamber surrounds the distal end portion of the tube and the openings the rein. A flexible material occupies said chamber and forms fluid connections between a selected part of an external surface of the chamber and the openings of the distal end portion of the tube. The selected part of the external surface of the chamber is adapted for contacting an external or internal surface portion of the internal body organ. Thereby, interstitial fluid of the internal body organ adjoining said selected part of the external surface of the chamber is sucked off from the internal body organ.

WO 03/028786 A2

A METHOD, A DEVICE, AND A SYSTEM FOR ORGAN RECONDITIONING AND A DEVICE FOR PRESERVING AN INTERNAL BODY ORGAN

Technical Field of the Invention

The present invention generally is related to reconditioning of internal body organs and more precisely is related to a device, a system and a method for reconditioning of an internal body organ having or risking a functional failure or impairment associated with a fluid collection therein. The present invention further relates to a device for preserving a body organ for transport purposes.

Background of the Invention

Functional failure or impairment of organ parenchyma is often caused by or associated with an increase of fluid, i.e. fluid collection which may cause a swelling, in the tissues (oedema). The fluid collection may cause a swelling, which in turn may result in a functional failure or impairment of an organ. However, a functional failure of an organ due to other causes may result in a fluid collection in the organ. The diseases causing these conditions may be very different. Infarctions, ischemia, and trauma may cause a situation where an increased amount of fluids leads to mal- or dysfunction of such internal body organs as the heart, the lungs, the kidney, the liver, the urinary tract, the guts, and the brain.

A heart infarction is caused by occlusions or blocks in the arteries of the heart. As a result of the block in the artery, a part of the heart will be deprived from nutrition and the heart muscle cells will die and go into necrosis. As a result of this process, water and other tissue fluids are accumulated in the diseased area of the organ. The increase of fluid in the organ tissue makes the diseased area or the whole organ stiff and a proper action of the heart muscle is inhibited.

Another situation when excessive fluid is present in the heart muscle is during the post cardiotomy syndrome, i.e. after extensive heart surgery when extra-corporeal circulation has been used and the heart has been arrested for a prolonged period of time.

A lung disease may also be impaired by excessive fluid in cases of infection, heart failure and shock. For shocked lungs, often called ARDS (adult respiratory distress syndrome), a major contribution to the failing function of the lungs is excessive fluid in the lung tissue.

The brain is an organ utterly sensitive to oedema and swelling. Since the skull represents a maximum volume, a swelling of the brain causes an immediate increase in the intracranial pressure. At a certain swelling status of the brain, the passage of blood and cerebral fluid is completely stopped through the foramen magnum, i.e. the opening into the skull.

Also, during organ preservation for transplant purposes oedema is a major concern, since accumulated fluid caused by ischemia and perfusion solutions inhibit good function immediately after transplantation and for the first post-operative period.

The normal transportation of fluids away from internal body organs is through the vascular system, basically through veins and the lymphatic system. Such fluid transportation through the vascular system is slow since fluids first have to be moved from the tissue between the organ cells into the vascular system along minimal gradients of osmotic pressure and capillary pressure.

Until now the single technique used for obtaining a faster reconditioning of a swollen internal body organ is general administrating of diuretics, a therapy that takes time and has disadvantages like electrolyte imbalance and dehydration of other parts of the body.

Summary of the Invention

Due to the above-mentioned problems, an object of the present invention is to provide a method, a device, and a system for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein.

This object is attained by means of a device and a method according to the appended independent claims. Preferred embodiments of the invention are stated in the dependent claims.

According to the invention there is provided a device for reconditioning of an internal body organ having, or risking a functional failure associated with a fluid collection therein, comprising: a tube having a proximal end adapted for connection to a vacuum source, and a distal end portion having a plurality of openings; a chamber surrounding the distal end portion of the tube and the openings therein; and a flexible material occupying said chamber and forming fluid connections between a selected part of an external surface of the chamber and the openings of the distal end portion of the tube, said selected part of the external surface of the chamber being adapted for contacting the internal body organ, whereby interstitial fluid of the internal body organ adjoining said selected part of the external surface of the chamber may be sucked off from the internal body organ.

Thus, the invention provides an increased fluid flow away from a swollen organ, thereby contributing to a faster reconditioning of the swollen organ.

According to another aspect of the invention, there is provided a device for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said device comprising: an organ contacting surface, which is adapted to contact the internal body organ, said organ contacting surface having, at least during the use

of the device, pores allowing interstitial fluids to flow from the internal body organ through the surface; and a draining element adapted to apply a negative pressure at the organ contacting surface and adapted to lead said interstitial fluids away from the internal body organ at said organ contacting surface via said pores.

According to the invention, there is also provided a system for reconditioning an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said system comprising

(i) an organ contacting device, said organ contacting device including:

- an organ contacting surface, which is adapted to contact the internal body organ, said organ contacting surface having pores allowing interstitial fluids to flow through the surface; and

- a draining element adapted to apply a negative pressure at the organ contacting surface and adapted to lead sucked off fluids away from the organ at said organ contacting surface; and

(ii) a negative pressure source for connection to the draining element and for creation of the negative pressure at the organ contacting surface.

Further, a method according to the invention for reconditioning an internal body organ having, or risking a functional failure associated with a fluid collection therein, comprises the steps of providing a tube, which has a proximal end and a distal end portion having a plurality of openings, a chamber surrounding the distal end portion of the tube and the openings therein, and a flexible material in said chamber and forming fluid connections to the openings of the distal end portion of the tube; contacting the internal body organ by said flexible material; and connecting the proximal end of the tube to a vacuum source, whereby interstitial fluid of the internal body organ adjoining said selected part of

the external surface of the chamber is sucked off from the internal body organ.

According to another aspect of the invention, a method for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein comprises the steps of contacting the internal body organ with a suction device, and creating a negative pressure in a contact area between the internal body organ and the suction device, whereby interstitial fluid is sucked off from the internal body organ.

According to a further aspect of the invention, a method for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein comprises the step of sucking off interstitial fluid from an external surface or from the interior of the internal body organ.

According to yet another aspect of the invention, a method for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein comprises the step of increasing fluid flow away from the internal body organ by applying a negative pressure to the internal body organ.

Accordingly, the present invention uses suction or gentle vacuum on the organ surface and thereby directs the fluid flow in a direction opposite to the normal fluid flow away from the organ, i.e. out of the organ through the outer layer of the organ surfaces, e.g. the epicardium, and the pleura of the lung. In comparison to the use of diuretics, a direct removal of excessive fluids from the organ surface will create neither electrolyte imbalance nor dehydration of other parts of the body. Further, the direct removal via the organ's surface will work fast, so that excessive fluid can be removed in an early stage of a disease. Thereby, a

chronic state with cell inflammation and scar tissue formation may be avoided.

Fluid collection in an organ implies that fluid is accumulated in cells and between cells of the organ. When a negative pressure is applied to the organ in accordance with the invention, interstitial fluid, i.e. fluid between the cells, will be sucked off from the organ. However, the sucking off of interstitial fluid will result in intracellular fluid, i.e. fluid within the cells, moving out from the cells by osmotic pressure, whereby this fluid may also be sucked off from the organ. The interstitial fluid is a liquid, but gases may accompany the fluid when it is sucked off. Further, the sucked off fluid may carry toxins and other inflammatory substances as well as free radicals away from the organ. The term "interstitial fluid" does not include blood or fluids in a body cavity outside organs.

The term "reconditioning" should be interpreted in a broad sense. In the present application, "reconditioning" will include not only the action of removing an existing fluid collection of an internal body organ but also the action of preventing an expected fluid collection of an internal body organ.

The feature that the chamber "surrounds" the distal end portion of the tube and the openings thereof implies that at least the openings will be covered by the chamber.

US 5,636,643 discloses a device for a completely different purpose than reconditioning of internal body organs. The device according to US 5,636,643 is used for treatment of wounds. The device comprises a tube for providing a suction, a wound screen for application on the wound and around a distal end of the tube. When the device is arranged on a wound and a negative pressure is applied to the wound, the healing of the wound will be stimulated and accelerated.

Further, US 6,015,378 discloses another device that also somewhat resembles the device according to the invention. The device according to US 6,015,378 is used for the purpose of stabilizing a tissue area. Thus, the device comprises a suction device and suction openings at a distal end of the suction device. When a negative pressure is applied to the suction device, a body tissue in the vicinity of suction openings will be immobilized by a suction force binding it to the suction opening.

According to an aspect of the invention, a special feature of the device and its surface towards the organ to be reconditioned is the properties of the surface to prohibit, or at least substantially reducing, stimulation of granulation tissue. Such granulation tissue is a specific tissue for healing of wounds and tissue damages, especially such damage that is caused by infections and burns. The application of an organ contacting surface in contact with an internal body organ may stimulate formation of unwanted granulation tissue, if the surface is not designed to prohibit this reaction. Granulation tissue contains tissue like capillaries, inflammatory cells and fibrocytes or fibroblasts. Such cells may originate from the blood or the tissue itself. Such wound healing reaction is unwanted during reconditioning by means of the device and the device is designed to avoid such reactions.

One way to avoid granulation at the surface is to choose material and/or porosity of the device surface such that the granulation tissue stimulation is avoided. Thus, the organ contacting surface may have pores of a size sufficiently small to prevent stimulation of granulation tissue formation. The pores of the organ contacting surface are preferably of a size in the interval 2-300 μm. It is even more preferred that the size of the pores is in the interval 2-4μm. In these intervals, the pores will be sufficiently big to allow interstitial fluids to flow through the surface, while

the pores still are sufficiently small to prevent stimulation of granulation tissue formation. Further, the pores will also be smaller than the size of the blood cells to prohibit exsanguination of the patient or sucking any parenchymal cells.

In other words, the pores of the flexible material may typically be of a size in the interval 2-300 μm at the selected part of the external surface of the chamber, since small pores will not stimulate granulation tissue generation as much as large pores.

The pores of the organ contacting surface may initially be clogged. Then, a negative pressure applied by the draining element will not affect the surroundings of the organ contacting surface but may instead be used for compressing the part of the device carrying the organ contacting surface, which is to be introduced into the body. Preferably, the pores are clogged by a resorbable material. Thus, the material clogging the pores may be resorbed when the organ contacting surface is introduced into the body. Then, the pores are cleared so that interstitial fluid may flow through the organ contacting surface when a negative pressure is applied by the draining element.

Also, since the surface prohibits, or at least substantially reduces, granulation tissue stimulation, the device may easily be replaced as it will not attach to the organ surface. Further, the device may be arranged for creating an overpressure to the body organ surface. The creation of an overpressure may be used for detaching the device from the body organ surface when the device is to be replaced or retrieved. In particular, the overpressure may be used for breaking any granulation tissue formations. An occasional overpressure may also be used for breaking any granulation tissue formations during the application of the device in contact with the body organ surface. This overpressure may be applied periodically.

Alternatively, the selected part of the external surface may comprise a material, drug or substance, that prohibits, or at least substantially reduces, adhesion and granulation tissue formation. Thus, an adhesion of the device to the body organ is prohibited.

Further, the method according to the invention may comprise the step of prohibiting, or at least substantially reducing, stimulation of granulation tissue at a contact area of the flexible material to the surface of the body organ, and/or the step of prohibiting, or at least substantially reducing, stimulation of adhesion of the contact area to the surface of the body organ.

Preferably, at least part of a peripheral surface of a porous body forms the organ contacting surface. Thus, the organ contacting surface provides an interface between a surface of a body organ and a porous body. The porous body may enable the application of a negative pressure at the organ contacting surface by coupling the draining element to the organ contacting surface. Peripheral parts of the porous body which do not form the organ contacting surface may be covered by a film. This may prohibit fluid flow into the porous body through other parts than the organ contacting surface.

The porous body may be flexible. This may be advantageous in that the porous body may then be shrunk by an applied negative pressure inside it, which will facilitate introduction of the porous body into a human body.

Preferably, a distal end of the draining element is arranged inside the porous body. Thus, the negative pressure may be applied through the porous body and sucked off fluids will be led through the porous body from the organ contacting surface to the draining element. The draining element may comprise a tube for leading away fluids. Preferably, the distal end of the draining element comprises at least one suction opening in the tube. Through this suction opening fluids may be

led away from the body organ by means of the applied negative pressure. In particular, the draining element may comprise a plurality of suction openings. These suction openings are preferably distributed in relation to the organ contacting surface. Thus, the negative pressure applied to the organ contacting surface may be uniformly distributed over the organ contacting surface. Preferably, the distal end of the draining element extends in the porous body substantially in parallel to the organ contacting surface. As a result, suction openings distributed over the length of the distal end will be distributed in relation to the organ contacting surface. The draining element may also be connectable to a vacuum source for providing the negative pressure to the organ contacting surface.

In a first embodiment, the selected part of the external surface of the chamber, or in other words the organ contacting surface, is adapted for contacting an external surface portion of the body organ. Thus, the body organ may be treated, while no penetration of the organ tissue is needed. According to this embodiment, a negative pressure may be applied to an external surface of the body organ for sucking off interstitial fluid.

Preferably, the non-selected part of the external surface of the chamber is impermeable to fluids. The non-selected part of the external surface of the chamber may also be impermeable to gases. Further, the non-selected part of the external surface of the chamber may comprise a film.

In the first embodiment, the device according to the invention may have a flat chamber with two opposing sides. Then, the selected part of the external surface of the chamber may be positioned on only one of the two opposing sides.

This embodiment is well suited for attaching the device to such organs as the heart, the lungs, the kidney, the liver, and the guts. The selected part of the

external surface of the chamber may be enclosed by a sealing ring, thereby ensuring a tight attachment. Preferably, the sealing ring comprises a sealing lip.

The device may also comprise means for creating a negative fixation pressure between the sealing ring and a surface of a body organ, whereby the sealing ring may be fixated to the surface of the body organ. For example, the sealing ring may have a U-shaped cross-section. If a negative pressure is applied, the U-shaped sealing ring will be fixated to a surface below the opening of the U-shape. Alternatively, the sealing ring may comprise several suction cups, which may be fixated to the surface of the body organ.

Also, the sealing ring is preferably impermeable to fluids and it may further also be impermeable to gases. This enables a tight fixation of the device to the body organ.

Also, the chamber may be divided into compartments. Each such compartment may comprise a portion of the selected part of the external surface of the chamber. In other words, the porous body may be divided into compartments, wherein part of a peripheral surface of each compartment form separate portions of the organ contacting surface. In this case, the tube may have a separate lumen for each compartment, or each compartment may have a separate tube for connection to a vacuum source. Thus, the draining element may have a separate lumen for each compartment, or may comprise several tubes, wherein each tube comprises a distal end arranged in one of the compartments. This configuration enables a varied suction across the surface of a treated organ.

Further, each compartment may have a sealing ring, preferably comprising a sealing lip, enclosing its portion of the selected part of the external surface of the chamber. In other words, a sealing ring may enclose each portion of the organ contacting surface. Also, the sealing ring of each compartment may comprise means for

creating a negative pressure between the sealing ring and a surface of a body organ, whereby the sealing ring may be fixated to the surface of the body organ. The sealing ring of each compartments may each comprise a sealing lip.

The selected part of the external surface of the chamber or the organ contacting surface is suitably covered by a perforated film. Then, the flexible material or the organ contacting surface will not be in direct contact with the surface of the organ, but still fluid connections could be formed.

The porous body may comprise a spongy material. Alternatively, the flexible material or, in other words, the porous body preferably comprises a web, which could comprise e.g. a synthetic tissue selected among the group consisting of polyester, polydioxanon, poly-hexafluoropropylen-VDF, polyglyconat, polyglycolic acid, polyglactin, and silicon. The web may also comprise a metal material, such as Nitinol. Alternatively, the web may comprise a combination of a metal and a synthetic material. These configurations of the flexible material or the porous body will enable fluid flow through the material. Also, the flexible material may be a resorbable material, thus enabling the flexible material to be left in the body after the treatment.

According to a further alternative, the web comprises at least one layer of a net. The net may be fine-meshed, thus forming pores of the web. The web might comprise several layers of net on top of each other creating a multi-layer net. The mesh size of the layers may then differ at the various levels allowing individual design for different organs and fine-tuning function.

Further, the selected part of the external surface of the chamber or the organ contacting surface preferably restrains shrinking due to a negative pressure in the tube creating a suction. This could be accomplished by a sealing ring sufficiently rigid to maintain its form

under the negative pressure. The sealing ring will then prohibit the selected part of the external surface from shrinking. Such shrinking and subsequent stiffness of the flexible material would be of definitive disadvantage when the device would be used e.g. on a beating heart. Also, the material of the distal end portion of the tube may restrain shrinking due to the negative pressure.

The resistance towards shrinking implies that the area of the selected part of the external surface may be held constant. Thus, the flexible material may have an essentially stable form in a plane of the selected part of the external surface, while being pliable such that the selected part of the external surface may be bent and formed to come in contact with a curved surface of the body organ. During this bending the area of the selected part of the external surface is not changed.

In a second embodiment, the selected part of the external surface of the chamber, or in other words the organ contacting surface, is adapted for contacting an interior portion of the body organ. Then, the selected part of the external surface may be brought in close proximity to a fluid collection in the body organ. According to this embodiment, a negative pressure may be applied to the interior of the body organ.

In this second embodiment, the device according to the invention may have a chamber, which is substantially cylindrical. Then, the selected part of the external surface of the chamber includes the peripheral part of the substantially cylindrical chamber, preferably the total external surface of the chamber. In other words, the porous body may be substantially cylindrical and at least part of the peripheral surface of the substantially cylindrical porous body may form the organ contacting surface.

Preferably, the device further comprises a delivering cannula, into which the chamber or porous body may be inserted in a compressed state. This enables a

simple introduction of the chamber into the body and to an organ to be reconditioned.

This embodiment is preferred for treatment of a swelling of the brain. By inserting a device according to this second embodiment of the invention into the brain tissue, oedemas may be treated before the above-described disastrous development occurs, such oedemas being the main cause of death after head injury, vascular disasters in the brain and after brain surgery. The device may be inserted through the skull bone where a screw will tighten the insertion hole and prohibit leakage, or through the vascular system, either through a vein or through an artery. The device may also be inserted into the skull under the bone but outside of the brain tissue, sucking on the brain surface, inside or outside the dura mater.

Such treatment inside the organ parenchyma (i.e. between the organ cells and not on an organ surface) may also be used in other organs, such as the heart or the kidneys. In such treatment inside the organ parenchyma, the pores of the selected surface is preferably selected in the interval of 2-4 μm, i.e. smaller than the size of the blood cells to prohibit exsanguination of the patient or sucking any parenchymal cells.

Since the processes of fluid increase in the heart may be very fast, the invention also provides for a monitoring of the function and the recovery of the heart muscle cells. If the monitoring discloses a need for immediate direct therapy, like electrical stimulation or D.C. shock, the device according to the invention may permit such action. The device may also permit localized distribution of drugs in the diseased tissue as well as direct pacemaker stimulation of the heart surface. The placement of the device on the heart surface may be done directly when the chest is opened, or it may be applied to the heart surface by percutaneous direct puncture into the pericardial space. The system may also be inserted

into the organ parenchyma by means of a percutaneous puncture technique through the skin directly into the pericardium or through the vascular system by veins or arteries.

Myocardial infarction is an event caused by sudden blocks in the arteries supporting a certain area of the muscle. The blocks are caused by blood clots, so called thromboses. The acute ischemia that occur causes death of heart muscle cells in the area and swelling by fluid collection caused by necrosis of the cells and oedema. The presented device is ideal for treatment of such areas of dead swollen muscle cells. If, however the block in the artery is opened by means of drugs, balloon dilatation or acute bypass surgery such cell death may be omitted or limited. However, immediately after restoring blood flow in the previously blocked areas the recurring blood flow causes so-called reperfusion damage, i.e an oedema in the ischemic area and also in the border zones of the ischemic area. Such oedema impair the myocardial contraction, but the presented device may cure such impairment instantly. If reopening the artery is unsuccessful cell death will occur and a border zone swelling will develop impairing also the surviving cells in the border zone. By applying the device in the swollen border zone the global function of the heart will improve as well as survival after the myocardial infarction. Ischemic areas next to necrotic myocardial cells are called stunned or hibernating myocardial tissue suffering from deficient blood support, these areas are also the areas causing the alarming and frightening pain of the unstable angina pectoris. The presented invention may cure such starvation of blood supply by means of another feature, that is its ability to increase blood flow in the small vessels called capillaries and arterioles in the stunned or hibernating areas. By clearing the area of superfluous fluid and by sucking in the venous end of the capillaries a passive blood supply may be created from

the adjacent healthy areas into the starved areas treated by the presented device.

By altering the suction modus in the device, efficiency of the device may be increased and thereby also an enhancement of the microcirculation may be created. Such altering typically would include a fine tuning of the suction force by tuning the applied negative pressure to an interval between 25 mmHg to 125 mmHg and also making the variation of suction force cyclic, e.g. increasing and decreasing suction at an interval of 1 - 3 minutes. Another feature of the present invention is that, in addition or instead of the 1 - 3 minutes variation of suction, a much faster variation of the suction force may be triggered by the detected electrocardiogram (ECG) to determine an optimal period to the variation in each cardiac cycle. Thus, the variation according to the ECG may be superposed on the 1 – 3 minutes variation, or alternatively control the whole variation. Typically the ECG triggered variation would peak the suction in the diastole of the heart cycle when the blood support of the left heart side is at its maximum. However the systole of the heart cycle may also be chosen for increasing the microcirculation in other areas of the heart, for instance the right side of the heart. It is obvious from what is mentioned above that such increase in the microcirculation in the ischemic areas causing pain may cure the very often intractable chest pain of unstable angina pectoris. It is also obvious that such an increase in microcirculation will salvage and supply heart muscle cells during a period of regeneration of blood vessels to the damaged area and thereby permit a permanent salvage of that heart muscle area.

Preferably, the device may further comprise an electrical current conducting means adapted for contacting the body organ. The electrical current conducting means may comprise at least one electrode. For instance, the electrical current conducting means may be

adapted for detecting an electrical current. Then, the electrical current conducting means may be adapted for detecting an electrical current in the body organ. This detection may be used for monitoring ECG signals of a heart.

The electrical current conducting means may also or alternatively be adapted for detecting an electrical current influenced by the fluid flow away from the body organ, e.g. by a change of conductivity. Thus, the flow of interstitial fluid sucked off from the body organ may be monitored. Monitoring the flow of interstitial fluid from the body organ gives a view of how fast the process of treating the body organ progresses. It may also indicate when the body organ needs no further treatment, i.e. when the flow is at a level corresponding to treatment of a healthy organ. Thus, a degree of vacuum in the vacuum source may be regulated in dependence of the monitored flow. Also, the vacuum source may be shut off when the monitored flow is at a normal level.

Further, the electrical current conducting means may be adapted for applying an electrical current to the body organ. In this case, the electrical current conducting means may comprise a net layer of metal for applying an electrical current to the body organ over a distributed surface. The net layer of metal may be arranged at the organ contacting surface. The electrical current conducting means may alternatively comprise a metal wire around the organ contacting surface for achieving a distributed application of an electrical current to the body organ. This may be used for electrical stimulation regulating the heart rhythm (pacemaker) or a D.C. shock to a heart, if this is needed during a treatment of the heart.

According to the invention, there is provided a device for preserving a body organ for transport purposes comprising: having a web inside; at least one tube having a proximal end adapted for connection to a vacuum source

and a distal end portion having a plurality of openings; a flexible sealed bag surrounding the distal end portion of the tube and the openings therein; and a flexible material positioned on the inside of the flexible bag, the openings in the distal end of the tube being positioned within the web, which forms fluid connections between an external surface of a body organ placed in the bag and the openings of the distal end portion of the tube, whereby interstitial fluid of the body organ adjoining the web is sucked off from the body organ.

According to another aspect of the invention, there is provided a device for preserving a body organ for transport purposes, said device comprising: a sealable bag having an internal space for receiving a body organ; and a draining element adapted to apply a negative pressure to an external surface of the body organ and adapted to lead sucked off fluids away from the body organ.

The transportation and storage period for organs to be transplanted may be used for reconditioning by use of the present invention. By treating the whole organ or the organ surface with gentle vacuum during transportation and storage, and also after transplantation, excessive oedemas may be extracted and a superior function of vacuum treated organs will be ensured. Such treatment may be very advantageous for kidney, livers, lungs and hearts intended for transplantation. The device has a sealable bag, whereby a suction may be provided to an organ in the bag. The draining element need not be in actual contact with the organ in order to apply the negative pressure for sucking off fluid from the organ.

Preferably, the device for preserving a body organ for transport purposes further comprises an organ contacting surface located within the bag and adapted to contact the body organ. The organ contacting surface may be connected to the draining element for applying a negative pressure to the external surface of the body

organ. The organ contacting surface may be used for applying the negative pressure to at least a part of the body organ and for forming fluid connections between the body organ and the draining element.

In the device for preserving a body organ for transport purposes, the organ contacting surface is preferably formed by a peripheral surface of a porous body. Further, the porous body may comprise a flexible material. Then, the porous body could conform to the shape of the organ in the bag. Also, the porous body may comprise a web.

The draining element of the device for preserving a body organ may comprise at least one tube and preferably comprises several tubes. At least one suction opening may be arranged at a distal end of each tube, which distal end may be arranged in the porous body. Thus, fluids may be sucked off from the body organ in the bag through the organ contacting surface, the porous body and the suction opening, whereby the fluids may be led away from the bag through the tube. Further, the draining element may be adapted for connection to a vacuum source for providing a negative pressure at the organ contacting surface.

Further, the device for preserving a body organ may be placed inside a cooling box or in a cooled environment to keep the organs at a lowered temperature. This enhances the preservation of the body organ.

Brief Description of the Drawings

Preferred embodiments of the invention will now be described referring to the appended drawings, wherein

Figs 1-3 are a top view, a side view and a bottom view of a first embodiment of a device according to the present invention.

Fig. 4 is a perspective view of a preferred embodiment of a sealing ring.

Figs 5-10 illustrate three further variants of a device according to the first embodiment of the present invention.

Figs 11-12 are a top view and a cross-sectional view of another variant of the device according to the first embodiment of the present invention.

Figs 13-14 are a top view and a cross-sectional view of still another variant of the device according to the first embodiment of the present invention.

Figs 15-16 illustrate the use of a device according to the present invention.

Fig. 17 illustrate two devices according to Figs 1-3 attached to the anterior wall of the heart and the backside of the heart.

Figs 18 and 19 illustrate the use of four devices according to Figs 13-14 for reconditioning of the lungs.

Figs 20-22 illustrate how a device according to Figs 1-3 may be minimized for insertion into a cannula.

Figs 23-25 illustrate a second embodiment of the device according to the present invention which are intended for insertion into the organ, i.e. an intraparenchymal device for insertion into the tissue of the organ.

Figs 26 and 27 are partial cross-sectional views of a skull and illustrate the use of the devices shown in Figs 23-25.

Figs 28-30 illustrate a third embodiment of a device according to the invention intended for preservation of a body organ for transplantation.

Figs 31-32 illustrate alternative embodiments of the sealing ring.

Fig. 33 illustrates a way of inserting the device according to Figs 1-3 into the body.

Detailed Description of Preferred Embodiments

The device illustrated in Figs 1-3 constitutes a first embodiment comprising a draining element having a

tube 1 with a proximal end 2 adapted for connection to a vacuum source (not shown), and a distal end portion 3 inserted into a flat chamber 4 having a flexible shape. A top side of the chamber 4 is covered by a thin film 5 which is impermeable to fluids and gases. The chamber 4 is filled by a flexible material 6 which may be a web, e.g. consisting of a synthetic tissue selected among the group consisting of polyester, polydioxanon (PDS), poly-hexafluoropropylen-VDF (Pronova), polyglyconat (Maxon), polyglycolic acid (Dexon), polyglactin (Vicryl), and silicon. It is the flexible material 6 of the chamber 4 that makes the shape of the chamber 4 flexible. However, the flexible material 6 permit the chamber 4 to reduce its volume when a negative pressure is applied. The flexible shape of the chamber 4 implies that the chamber may be bent and flexed to adapt to the form of an organ surface. However, a surface of the chamber 4, which is to be in contact with the organ, is essentially form stable, i.e. it may be bent but the area of the surface may not be compressed.

The web might also be created by putting nets of the materials mentioned on top of each other creating a multi-layer net. However, only a few or even only one layer may be used. The size of the masks in the net may then differ at the various levels allowing individual design for different organs and fine tuning function. The web may also be made of metal in form of metal sheets with masks in one or multiple layers, or alternatively it may also be made of one or multiple thin threads of metal distributed in a predetermined manner or at random. Typically, one such metal would be Nitinol, i.e. an alloy of nickel and titanium with inherent shape memory function. However, a combination of one or more of the synthetic materials and metal may also be used.

The flexible material 6 comprises pores and openings. Therefore, gases and fluids may be transported through the flexible material 6. Preferably, the pores of

the flexible material are of a size smaller than 300 µm, since this prohibits, or at least substantially reduces, stimulation of granulation tissue creation when the flexible material 6 comes in direct contact with an organ surface, as described above.

The draining element could alternatively be described as having a porous body and a tube, wherein a distal end portion of the tube is arranged within the porous body.

The distal end portion 3 of the tube 1 has at least one, but preferably a plurality of holes 7 or suction openings. If several holes 7 are arranged in the tube 1, it is not so critical if a hole 7 is clogged. The flexible material 6 in the chamber 4 forms fluid connections through its pores. Thus, fluid connections are formed between these holes 7 and a selected part 8 of an external surface of the chamber 4. The selected part 8 of the external surface of the chamber 4 may also be described as an organ contacting surface formed by a peripheral surface of the porous body. In Fig. 3 this selected part is illustrated as part of the bottom side of the chamber 4. The flexible material 6 may be exposed within the selected part 8 of the external surface of the bottom side of the chamber 4, or it may be covered by a perforated film.

The selected part 8 of the external surface of the chamber 4 is permeable to fluids, whereby the fluid connections could be formed. Also, the selected part 8 of the external surface may be seeded or covered with a material, drug or substance, that is prohibitive against adhesion and stimulation of granulation tissue. Such material or substance may be silver or carbon, but any other substance that is accepted by the human body and have the same effect might be used. Drugs with such effects are typically steroids, anti-inflammatory drugs like ibubrufen and similar drugs, and also cytostatic agents and cytotoxic agents.

The holes 7 are preferably formed on a side of the distal end portion 3 of the tube 1 proximal to the selected part 8 of the external surface of the chamber 4. The distal end of the tube 1 is preferably closed so that the vacuum source could create a suction through the holes 7. Preferably, the holes 7 in the tube 1 are distributed in relation to the selected part 8 of the external surface of the chamber 4 such that a substantially uniform negative pressure may be applied at the selected part 8 of the external surface. The distribution of the holes 7 may also be used for achieving a controlled variation of the negative pressure over different parts of the selected part 8 of the external surface.

The pores of the organ contacting surface or of the selected part 8 of the external surface may initially or temporarily be filled by a biodegradable or resorbable material. Alternatively, the selected part 8 of the external surface may be covered completely by a film of a resorbable material.

Thus, if a negative pressure is applied through the tube to the chamber or porous body, it will be compressed to a very small size, since air in the flexible material could be sucked away through the tube. This is possible since the surface of the chamber is tight as the pores of the surface are filled by a resorbable material. This may advantageously be used for insertion of the device into contact with the body organ. When the surface is arranged in contact with the body organ, the resorbable material will be resorbed or decomposed. With open pores the device will swell to its natural size, whereby fluid flow through the pores of the selected part 8 of the external surface is once again enabled. This implies that the device may be inserted into the body in a very small size and then suction of fluids through the device will automatically be enabled in the body. The resorbable material could be PDS (polydioxanon), Pronova

(polyhexafluoropropylen-VDF), Maxon (polyglyconat), Dexon (polyglycolic acid), Vicryl (polyglactin), any kind of saccaride, or human albumin.

The selected part of the bottom surface of the chamber 4 is enclosed or surrounded by a sealing ring 9, which in a preferred embodiment comprises a sealing lip, illustrated in Fig. 4. The sealing lip has a slack extension towards the chamber 4. A negative pressure in the chamber 4 will support fixation of this extension to a surface under it.

When a negative pressure is applied to the chamber 4, the sealing ring 9 is sufficiently rigid to restrain shrinking of the selected part 8 of the external surface of the chamber 4. Thus, the application of a negative pressure will not cause shrinking of the body organ, which otherwise could affect the function of the body organ negatively.

Referring to Figs 31-32, the sealing ring 9 could also be connected to a further vacuum source (not shown) for fixating the sealing ring 9 to a body organ by suction. Thus, the sealing ring 9, on its external surface which is to be in contact with the body organ, could e.g. comprise holes 31, suction cups, or have a U-shaped cross-section 32 with the opening towards the body organ when the device is applied in contact with the organ. This hole 31, suction cup or U-shaped cross-section 32 is then connected to the vacuum source for creating a negative pressure between the opening of the sealing ring 9 and the body organ and thus attaching the sealing ring 9 to the body organ.

The selected part 8 of the external surface of the chamber 4 is adapted for contacting an external surface portion of a body organ. When connecting the proximal end of the tube 1 to a vacuum source, the pressure within the chamber 4 could be decreased such that the chamber 4 will be tightly fixed against the external surface of the body organ by means of the sealing ring 9, while the flexible

material 6 in the chamber 4 will prevent the chamber from deflating. The sealing ring 9 will thus be tightly fitted to the surface of the body organ. A closed space is defined for creating a negative pressure on the surface of the body organ. The pressure decrease will generate a suction effect on the external surface of the body organ inside the sealing ring 9, whereby interstitial fluid of the body organ adjoining said selected part 8 of the external surface of the chamber 4 is sucked off from the body organ.

The proximal end 2 of the tube 1 will be connected to the vacuum source outside the body. However, the vacuum source need not be connected to the proximal end of the tube 1 but could also be connected to a proximal connecting portion outside the body. The proximal connecting portion need not be formed in the end of the tube; instead it may e.g. be in a proximal branch of the tube.

The fluid extracted from the body organ will be separated into a receptacle (not shown) connected into and interrupting the tube 1 between its distal and proximal ends.

Alternatively, the flexible material 6 may consist of any material separating the film 5 forming the top side of the chamber 4 and a perforated film forming the bottom side, or at least the selected part 8 of the bottom side of the chamber 4. Examples of such separating material are shown in Figs 5-10 as a plurality of tabs A, a honeycomb structure B and a spiral of a plastic tubing C, respectively. In these variants, the flexible material 6 is a structure with holes or openings. These holes or openings of the flexible material 6 will then form the fluid connections between holes in the perforated film and the suction openings 7.

Figs 11-12 illustrate a variant of the first embodiment of the device illustrated in Figs 1-3. However, the chamber 4 is separated into three different

compartments 10, 11 and 12, each one of the compartments 10-12 comprising a portion of the selected part 8 of the external surface of the chamber 4. Further, each compartment has a separate tube 1, 1', 1" leading to a vacuum source (not shown). Alternatively, there may be a single tube having a separate lumen or opening for each compartment. Each one of the compartments 10-12 may have a sealing ring 9, 9' and 9" enclosing its portion of the selected part 8 of the external surface of the chamber 4.

Obviously, by separating the chamber 4 into several compartments it is possible to vary the pressure across the surface of the body organ covered by the selected part 8 of the external surface of the chamber 4.

Each one of the sealing rings 9, 9' and 9" may be such a sealing lip as illustrated in Fig. 4. These lips may even extend to the top side film 5 and thus separate the compartments 10-12.

Metal contact points in the form of electrodes 13 are shown in Figs 11-12 as are wires 14. The wires 14 may connect the electrodes 13 to a detecting unit for recording ECG signals or to a pacemaker for stimulating purposes, when the device is fixed on a heart, as shown in Fig. 17. As stated above, the device according to the invention may permit immediate direct therapy, like electrical stimulation or D.C. shock, if the monitoring discloses a need for such action.

The electrodes 13 may be used for detecting an electrical current. This may be accomplished by having two spaced apart electrodes 13, which detect a current between them. The detection may be used for monitoring a current in the body organ, such as ECG signals. Through this detection the condition of the organ that is being treated may be monitored.

The detection may also be used for monitoring the flow of interstitial fluid sucked off from the organ by recording the change in conductance induced by the fluid flow. By monitoring the flow of fluid sucked off from the

organ the treatment of the organ may be controlled. The applied negative pressure may be regulated in response to recorded changes in the fluid flow. For example, when the fluid flow falls to a level of the fluid flow from a healthy organ, an indication is given that no further treatment is needed at that moment.

Further, a metal contact surface may be used for applying a current to the body organ. The electrodes 13 used for detection may also be used for this purpose, or alternatively separate metal contacts are arranged for this purpose. The metal contact surface may in this case be arranged as a net layer of metal, which also may form the organ contacting surface 8. This enables application of a current to the body organ over a distributed area. Alternatively, the metal contact surface may be arranged as a metal wire around parts or the whole organ contacting surface 8.

Figs 13-14 illustrate a variant of the device which substantially corresponds to the embodiment illustrated in Figs 1-3. However, the sealing ring 9 consists of a more rigid but still flexible ring and the chamber 8 has a rectangular shape instead of the oval shape shown in Figs 1-3. As in the embodiment of Figs 1-3, the tube 1 has a plurality of openings 7 in the distal end portion 3, and as in the variant shown in Figs 11-12, there are two electrodes 13 and two wires 14.

Fig. 15 illustrates a device according to the invention positioned on the tissue surface of a body organ with no suction applied. Fig. 16 illustrates the device in Fig. 15 with suction applied. The reduced pressure in the chamber 4 will compress the chamber 4 and give a suction effect on the tissue surface. As may be seen from Fig. 16, the compression of the chamber will not shrink the external surface of the chamber 4 in contact with the body organ in the plane of the surface. Thus, the part of the body organ in contact with the chamber 4 will not be immobilized by the suction.

Fig. 17 specifically illustrates the use of the device on a heart. In this application the device could be used for reconditioning a heart which e.g. suffers from ischemic areas caused by a myocardial infarction or from post cardiotomy syndrome.

In Figs 18-19 four devices according to Figs 13-14 are used for reconditioning of the lungs. Fig. 18 is a front view and Fig. 19 is a cross-sectional view along the lines XIX-XIX. Such application of the device could advantageously be used for treatment of e.g. ARDS, where excessive fluids is collected in the lungs.

Figs 20-22 are cross-sectional views of the device shown in Figs 1-3. In Fig. 20 the device is folded along a centre line so that the sealing lips along opposite edges of the chamber 4 get in contact with each other, as shown in Fig. 21. Then the suction from the vacuum source is applied via the tube 1, whereby the device will shrink further to a minimal size, as illustrated in Fig. 22, permitting easy insertion into and through a cannula or tube. The cannula could then be used for introduction of the device into the body in a compressed state. The device may alternatively be rolled to form a cylindrical shape for insertion into the cannula.

As shown in Fig. 33, the device may alternatively be rolled around a guide wire 33 or a tube for insertion. Suction from the vacuum source may shrink the device to a small size around the guide wire 33. When the device has been inserted to the desired position within the body, it may be rolled off the guide wire 33 or tube and subsequently be used for sucking off fluids from the body organ.

An intraparenchymal device for insertion into the tissue of an organ is illustrated in Figs 23-25. This device has the same tube 1 as the device shown in Figs 1-3, but its chamber 15 is substantially cylindrical and totally occupied by a flexible material 16. More precisely, the chamber 15 may be defined by the

peripheral surface of the flexible material 16 itself or may comprise a film which is perforated across a selected part of its external surface. Preferably, the selected part of the external surface of the chamber 15 includes the total peripheral part of the chamber 15.

The tube 1 may extend through the chamber 15, in which case the distal end of the tube 1 preferably is closed. Further, the tube 1 may have a permanent fixation to the flexible material 16 or it may be detachable by means of a quick connection coupling 17, as illustrated in Fig. 24. In this case, the flexible material 16 preferably is a resorbable material.

The flexible material 16 may be compressed so as to fit inside a cannula 18 for the delivery of the device. This delivery can be done by means of a piston 19, as illustrated in Fig. 25.

In Fig. 26, the intraparenchymal device according to Fig. 23 is inserted into the brain tissue. A special screw 20 fitting exactly to the suction tube 1 guarantees a tight sealing to the skull bone. In Fig. 27, the intraparenchymal device according to Fig. 23 is inserted under the skull bone either inside or outside the dura mater.

The device according to the present invention can be inserted directly or percutaneously by means of punction. Direct placement is done in the cases where direct access to the body organ in question is possible. Such direct placement would be possible in cases of open surgery where the surface of the body organ is exposed. Especially important is such direct placement during heart surgery and brain surgery when organs start to swell. Another situation when direct placement is possible is during transplantation of organs, after harvesting.

Special versions of the device are available for insertion and placement directly through the skin either by puncture or small incisions. The suction part of the

device, i.e. the holes 7 of the distal end portion 3 of the tube 1 and the chamber 4 surrounding them, may then be compressed in different ways around the tube to make it as small as possible. One way to make the suction part small is to cover that part of the device with a film that is retractable, and then apply suction, whereby the device will be extremely slim and small.

Thus, the intraparenchymal device permits treatment of organs from the inside tissue of the organs rather than from the external surface thereof. When the device is implanted into the tissue, a film around the web is in this case not necessary. The web or parts thereof will be retrieved, when the device is pulled out of the organ. If a detachable tube is used, the web material preferably is resorbable in the body organ.

A method for reconditioning of a body organ comprises insertion of a device, which is described above, into contact with the organ. The chamber 4 surrounding the distal end portion 3 of the device could be compressed and inserted into a cannula so that it may easily be inserted into the body by key-hole surgery, or by catheter technique. When brought to the body organ to be reconditioned, the device is released from the cannula and the chamber 4 may be brought into contact with a surface of the body organ. The selected part 8 of the external surface and the sealing ring 9 enclosing it will be brought in contact with the surface of the body organ. When a negative pressure is applied, interstitial fluids of the body organ will be sucked off from the organ through fluid connections in the flexible material 6 of the chamber 4, through the suction openings 7 of the tube 1 and through the tube 1 into a receptacle outside the body. Thus, the flow of excessive fluid from the body organ is increased and the body organ is reconditioned.

The fluid which is sucked off the body organ typically comprises electrolytes, such as salt and water. None or at least insignificant amounts of proteins or

cells are removed from the body organ with the fluid flow.

The applied negative pressure may be varied over different compartments 10-12 of the chamber 4 for varying the sucking off of fluids between different areas of the body organ. Further, the applied negative pressure may be varied in time. This may increase the efficiency of sucking off fluids, and thereby increase the efficiency of the device. Thus, the a cyclic variation of the applied negative pressure may be used, e.g. with a period of 1 - 3 minutes. Also, a much faster variation of the applied negative pressure may be triggered by the detected ECG as described above. This ECG-controlled variation may be used in stead of or in addition to the 1 - 3 minutes variation.

The applied negative pressure used is within the range of negative pressure used in the medical area, i.e. from 0 to 300 mmHg. Preferably, the applied negative pressure is within the range 25-125 mmHg.

Further, the device may be arranged so that a positive pressure may also be applied to the surface of the body organ. Thus, intermittently a positive pressure may be applied for a short period in order to break any granulation tissue that has been formed. Thereby, adhesion of the device to the surface of the body organ may be avoided.

The formation of granulation tissue may also be avoided by at certain intervals replacing the device in contact with the body organ. When the device is to be replaced a positive pressure might be applied so that any formed granulation tissue is broken.

Figs 28-29 illustrate another embodiment of a device according to the present invention for carrying a body organ intended for transplantation. The device comprises a completely sealed soft synthetic bag 21 surrounding a web 22, into which several tubes 1, 1', 1" extend. The end portions 23 of the tubes 1, 1', 1" within the bag 21

has a plurality of openings 7 in the web 22, such that the atmosphere in the bag 21 may be evacuated by means of a vacuum source connected to the external ends of the tubes 1, 1', 1". As illustrated in Fig. 30, a heart placed in the bag 21 will be contacted by the web 22 on the inside of the bag 21 substantially all over its external surface, when the pressure in the bag 21 is decreased, whereby the preservation of the heart is improved during transport and storage thereof. During the transport the bag preferably is immersed in a cool transportation fluid or kept in a refrigerator or a cooling box. Further, a temperature probe 24 inside the bag permits constant monitoring of the organ temperature.

For the man skilled in the art it is obvious that the device may be modified in several aspects in order to be used for other organs, like the guts, the kidneys, the urinary tract and the liver. Also, the device may be brought in contact with both an internal and an external surface of the body organ simultaneously.

Further, the organ contacting surface need not be the only part of the device which is in contact with the body organ. The device may have other parts in contact with the body organ, through which no suction of interstitial fluids is created. The device may also be arranged such that the organ contacting surface is divided into separate parts, through all of which a suction of interstitial fluids may be created.

CLAIMS

1. A device for reconditioning an internal body organ having or risking a functional failure associated with a fluid collection therein, said device comprising

a tube having a proximal end adapted for connection to a vacuum source, and a distal end portion having a plurality of openings,

a chamber surrounding the distal end portion of the tube and the openings therein, and

a flexible material occupying said chamber and forming fluid connections between a selected part of an external surface of the chamber and the openings of the distal end portion of the tube, said selected part of the external surface of the chamber being adapted for contacting the internal body organ,

whereby interstitial fluid of the internal body organ adjoining said selected part of the external surface of the chamber is sucked off from the internal body organ.

2. A device for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said device comprising:

an organ contacting surface, which is adapted to contact the internal body organ, said organ contacting surface having, at least during the use of the device, pores allowing interstitial fluids to flow from the internal body organ through the surface, and

a draining element adapted to apply a negative pressure at the organ contacting surface and adapted to lead said interstitial fluids away from the internal body organ at said organ contacting surface via said pores.

3. A device as claimed in claim 2, wherein said pores of the organ contacting surface are initially clogged.

4. A device as claimed in claim 3, wherein the pores are clogged by a resorbable material.

5. A device as claimed in any one of claims 2-4, wherein the organ contacting surface is adapted to contact an external surface portion of the body organ.

6. The device as claimed in any one of claims 2-5, wherein the organ contacting surface has pores of a size sufficiently small to prevent stimulation of granulation tissue formation.

7. The device as claimed in any one of claims 2-6, wherein the pores of the organ contacting surface are of a size in the interval 2-300 μm.

8. The device as claimed in any one of claims 2-7, wherein the pores of the organ contacting surface are of a size in the interval 2-4 μm.

9. The device as claimed in any one of claims 2-8, wherein the organ contacting surface has an essentially stable form.

10. The device as claimed in claim 9, wherein the organ contacting surface is pliable.

11. The device as claimed in any one of claims 2-10, wherein the organ contacting surface restrains shrinking during suction.

12. The device as claimed in any one of claims 2-11, wherein the organ contacting surface is covered by a perforated film.

13. The device as claimed in any one of claims 2-12, wherein at least part of a peripheral surface of a porous body forms the organ contacting surface.

14. The device as claimed in claim 13, wherein the porous body is flexible.

15. The device as claimed in claim 13 or 14, wherein the porous body comprises a spongy material.

16. The device as claimed in claim 13 or 14, wherein the porous body comprises a web.

17. The device as claimed in claim 16, wherein the web comprises a synthetic tissue selected among the group

consisting of polyester, polydiaxon, polyhexafluoropropylen-VDF, polyglyconat, polyglycolic acid, polyglactin, and silicon.

18. The device as claimed in claim 16, wherein the web comprises a metal material.

19. The device as claimed in claim 18, wherein the web comprises a Nitinol material.

20. The device as claimed in claim 16, wherein the web comprises a combination of a metal and a synthetic material.

21. The device as claimed in claim 16, wherein the web comprises at least one layer of a net.

22. The device as claimed in claim 21, wherein the net is fine-meshed.

23. The device as claimed in any one of claims 13-22, wherein peripheral parts of the porous body not forming the organ contacting surface are covered by a film.

24. The device as claimed in any one of claims 13-23, wherein a distal end of the draining element is arranged inside the porous body.

25. The device as claimed in claim 24, wherein the draining element comprises a tube.

26. The device as claimed in claim 25, wherein the distal end of the draining element comprises at least one suction opening in the tube.

27. The device as claimed in any one of claims 13-26, wherein the draining element is connectable to a vacuum source.

28. The device as claimed in any one of claims 13-27, further comprising a sealing ring, which encloses the organ contacting surface.

29. The device as claimed in claim 28, wherein the sealing ring is impermeable to fluids.

30. The device as claimed in claim 29, wherein the sealing ring is impermeable to gases as well.

31. The device as claimed in any one of claims 28-30, further comprising means for creating a negative pressure between the sealing ring and a surface of the body organ, whereby the sealing ring may be fixated to the surface of the body organ.

32. The device as claimed in any one of claims 28-31, wherein the sealing ring comprises a sealing lip.

33. The device as claimed in any one of claims 13-32, wherein the porous body is divided into compartments, part of a peripheral surface of each compartment forming separate portions of the organ contacting surface.

34. The device as claimed in claim 33, wherein the draining element has a separate lumen for each compartment.

35. The device as claimed in claim 33, wherein the draining element comprises several tubes, wherein each tube comprises a distal end arranged in one of the compartments.

36. The device as claimed in any one of claims 33-35, wherein a sealing ring encloses each portion of the organ contacting surface.

37. The device as claimed in claim 36, further comprising means for applying a negative pressure to each sealing ring.

38. The device as claimed in claim 36 or 37, wherein each sealing ring comprises a sealing lip.

39. A device as claimed in claim 13, wherein the organ contacting surface is adapted to contact an interior portion of the body organ.

40. The device as claimed in claim 39, wherein the porous body is substantially cylindrical and at least part of the peripheral surface of the substantially cylindrical porous body forms the organ contacting surface.

41. The device as claimed in claim 40, wherein the porous body comprises a resorbable material.

42. The device as claimed in claim 40 or 41, wherein the device further comprises a delivering cannula, into which the porous body is inserted in a compressed state.

43. The device as claimed in any one of claims 2-42, further comprising an electrical current conducting means adapted for contacting the body organ.

44. A device as claimed in claim 43, wherein the electrical current conducting means comprises at least one electrode.

45. A device as claimed in claim 43 or 44, wherein the electrical current conducting means is adapted for detecting an electrical current.

46. A device as claimed in claim 45, wherein the electrical current conducting means is adapted for detecting an electrical current in the body organ.

47. A device as claimed in claim 45, wherein the electrical current conducting means is adapted for detecting an electrical current influenced by the fluid flow away from the body organ.

48. A device as claimed in claim 43, wherein the electrical current conducting means is adapted for applying an electrical current to the body organ.

49. A device as claimed in claim 48, wherein the electrical current conducting means comprises a net layer of metal for applying an electrical current to the body organ over a distributed surface.

50. A system for reconditioning an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said system comprising

an organ contacting device, said organ contacting device including

an organ contacting surface, which is adapted to contact the internal body organ, said organ contacting surface having pores allowing interstitial fluids to flow through the surface, and

a draining element adapted to apply a negative pressure at the organ contacting surface and adapted to lead sucked off fluids away from the internal body organ at said organ contacting surface, and

a negative pressure source for connection to the draining element and for creation of the negative pressure at the organ contacting surface.

51. A method for reconditioning an internal body organ having or risking a functional failure associated with a fluid collection therein, comprising the steps of

providing a tube, which has a proximal end and a distal end portion having a plurality of openings, a chamber surrounding the distal end portion of the tube and the openings therein, and a flexible material in said chamber and forming fluid connections to the openings of the distal end portion of the tube;

contacting the internal body organ by said flexible material; and

connecting the proximal end of the tube to a vacuum source,

whereby interstitial fluid of the internal body organ adjoining the flexible material is sucked off from the internal body organ.

52. A method as claimed in claim 51, wherein the suction provided by the vacuum source is cyclically varied.

53. A method as claimed in claim 52, wherein the cyclical variation has an interval of 1-3 minutes.

54. A method as claimed in 52 for reconditioning of a heart, wherein the suction is varied in response to the electrocardiogram.

55. A method as claimed in any one of claims 51-53 for curing an unstable angina pectoris.

56. A method as claimed in any one of claims 51-53 for increasing the blood flow in the treated body organ.

57. A method as claimed in any one of claims 51-56, wherein the applied suction corresponds to a pressure of 25-125 mmHg.

58. A method as claimed in any one of claims 51-57, further comprising the step of prohibiting, or at least substantially reducing, stimulation of granulation tissue at a contact area of the flexible material to the surface of the body organ.

59. A method as claimed in any one of claims 51-58, further comprising the step of prohibiting, or at least substantially reducing, stimulation of adhesion of the contact area to the surface of the body organ.

60. A method as claimed in any one of claims 51-59, further comprising the step of monitoring the flow of interstitial fluid sucked off from the body organ.

61. A method as claimed in claim 60, further comprising the step of regulating a degree of vacuum in the vacuum source in dependence of the monitored flow.

62. A method as claimed in claim 60 or 61, further comprising the step of shutting off the vacuum source when the monitored flow is at a normal level.

63. A method as claimed in any one of claims 51-62, further comprising the step of detecting an electrical current in the body organ.

64. A method for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said method comprising the steps of:

contacting the internal body organ with a suction device, and

creating a negative pressure in a contact area between the internal body organ and the suction device,

whereby interstitial fluid is sucked off from the internal body organ.

65. A method for reconditioning of an internal body organ having, or risking a functional failure or

impairment associated with a fluid collection therein, said method comprising the step of:

sucking off interstitial fluid from an external surface or from the interior of the internal body organ.

66. A method for reconditioning of an internal body organ having, or risking a functional failure or impairment associated with a fluid collection therein, said method comprising the step of:

increasing interstitial fluid flow away from the internal body organ by applying a negative pressure to the internal body organ.

67. A method as claimed in claim 66, further comprising the step of applying a negative pressure to an external surface of the body organ.

68. A method as claimed in claim 66, further comprising the step of applying a negative pressure to the interior of the body organ.

69. A device for preserving a body organ for transport purposes, said device comprising

having a web inside,

at least one tube having a proximal end adapted for connection to a vacuum source, and a distal end portion having a plurality of openings,

a flexible sealed bag surrounding the distal end portion of the tube and the openings therein, and

a flexible material positioned on the inside of the flexible bag, the openings in the distal end of the tube being positioned within the web, which forms fluid connections between an external surface of a body organ placed in the bag and the openings of the distal end portion of the tube,

whereby interstitial fluid of the body organ adjoining the web is sucked off from the body organ.

70. A device for preserving a body organ for transport purposes, said device comprising:

a sealable bag having an internal space for receiving a body organ, and

a draining element adapted to apply a negative pressure to an external surface of the body organ and adapted to lead sucked off fluids away from the body organ.

71. The device as claimed in claim 70, further comprising an organ contacting surface located within the bag and adapted to contact the body organ, said organ contacting surface being connected to the draining element for applying a negative pressure to the external surface of the body organ.

72. The device as claimed in claim 71, wherein the organ contacting surface is formed by a peripheral surface of a porous body.

73. The device as claimed in claim 72, wherein the porous body comprises a flexible material.

74. The device as claimed in claim 72, wherein the porous body comprises a web.

75. The device as claimed in any one of claims 72-74, wherein the draining element comprises at least one tube.

76. The device as claimed in claim 75, wherein at least one suction opening is arranged at a distal end of each tube.

77. The device as claimed in claim 76, wherein the distal end of each tube is arranged in the porous body.

78. The device as claimed in any one of claims 70-77, wherein the draining element is adapted for connection to a vacuum source.

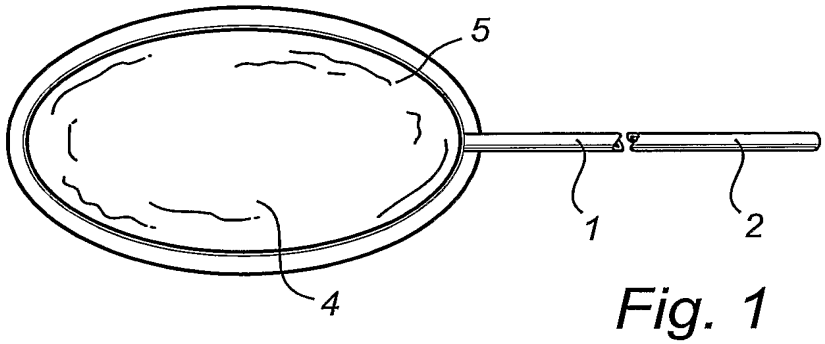


Fig. 1

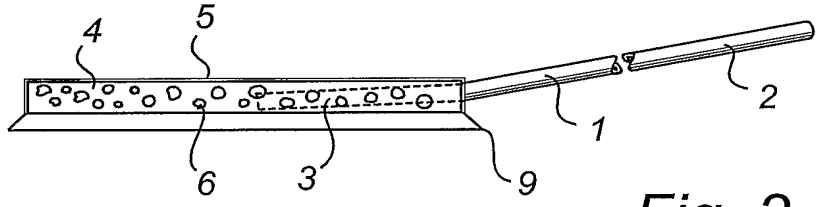


Fig. 2

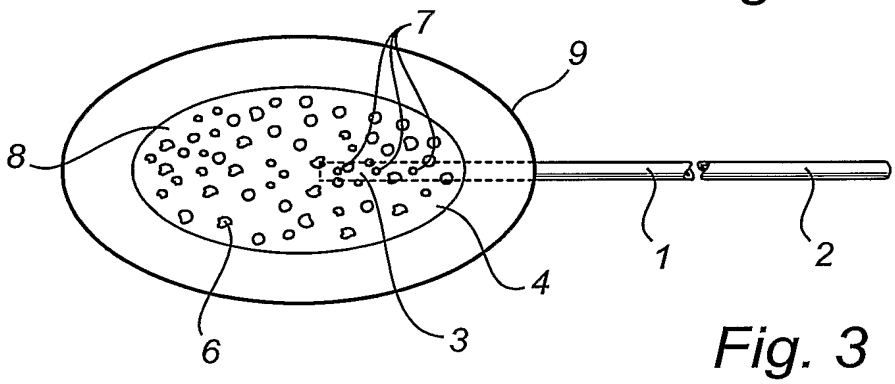


Fig. 3

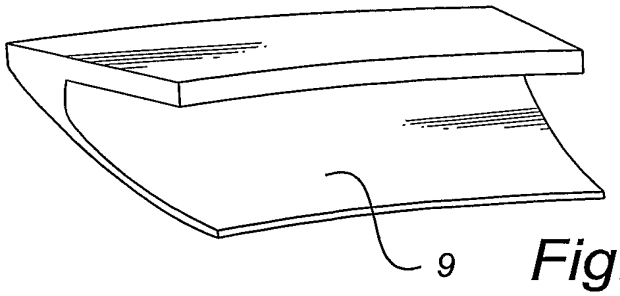


Fig. 4

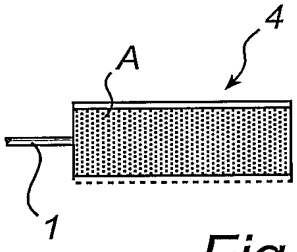


Fig. 5

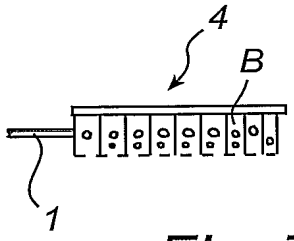


Fig. 7

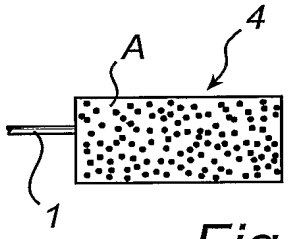


Fig. 6

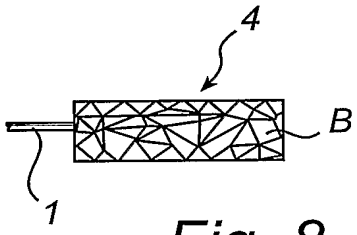


Fig. 8

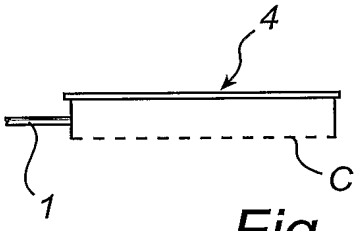


Fig. 9

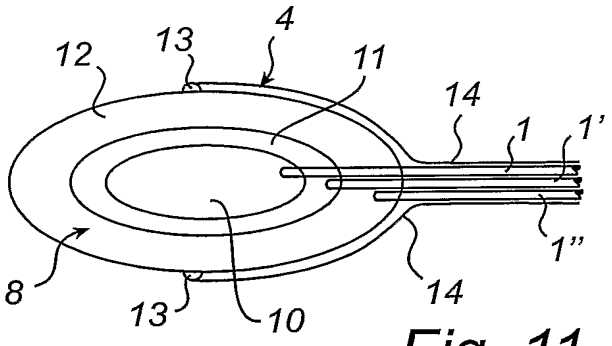


Fig. 11

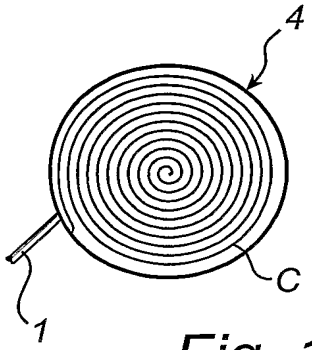


Fig. 10

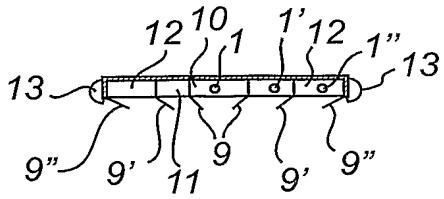


Fig. 12

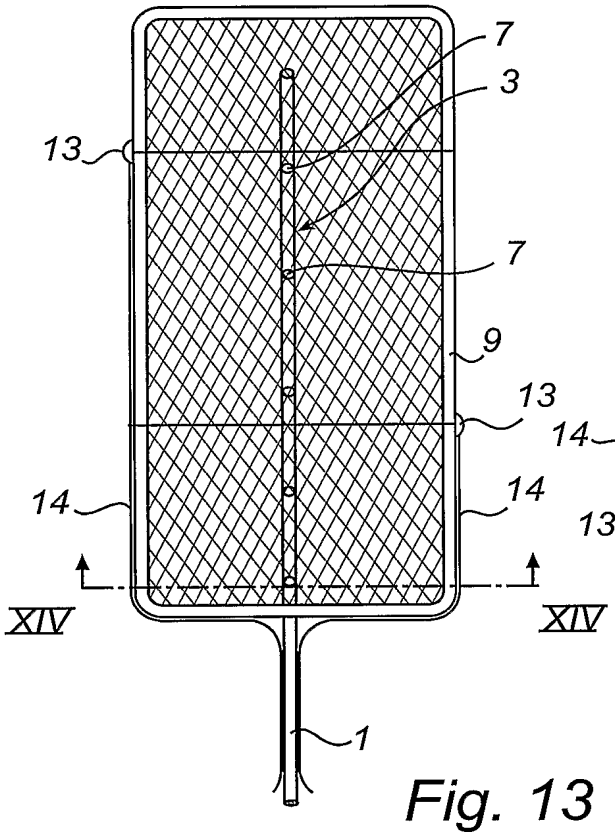


Fig. 13

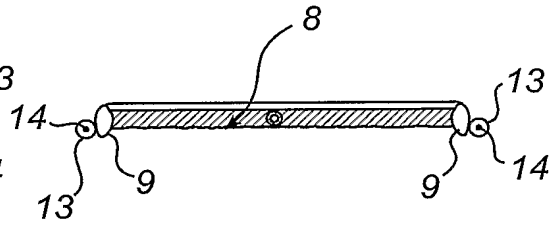


Fig. 14

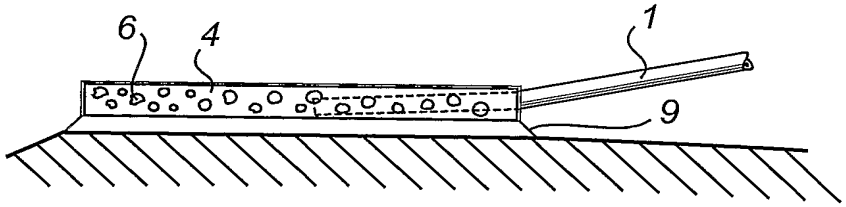


Fig. 15

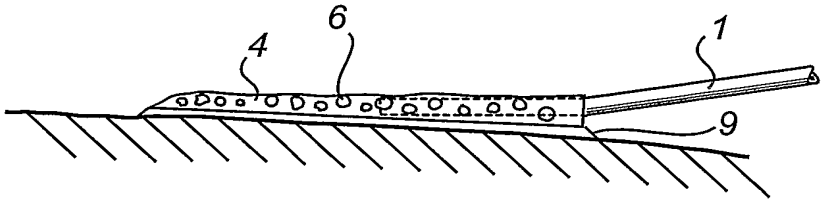


Fig. 16

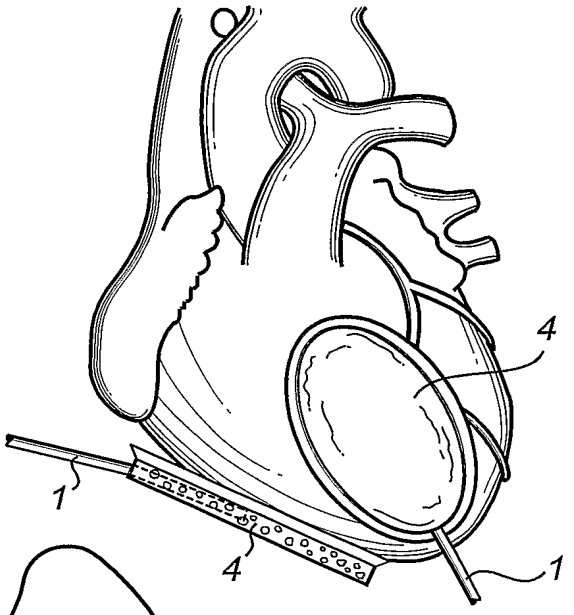


Fig. 17

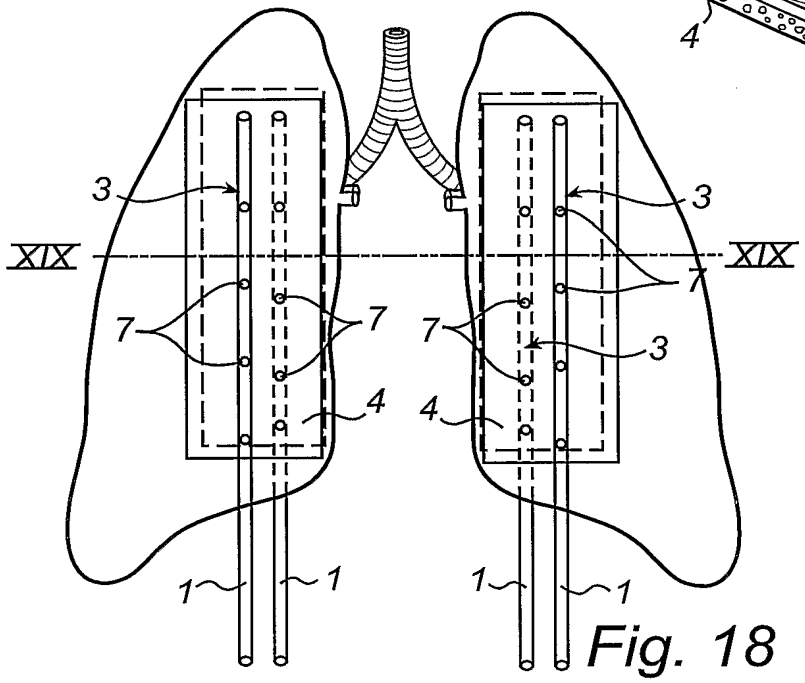


Fig. 18

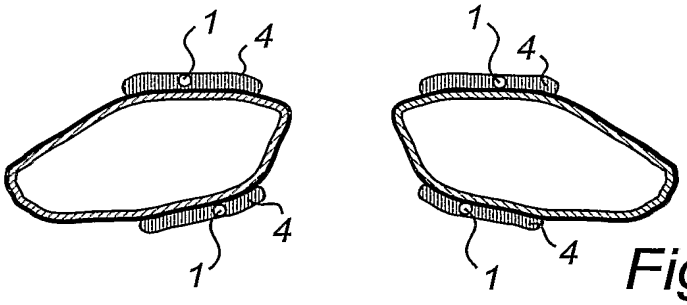


Fig. 19

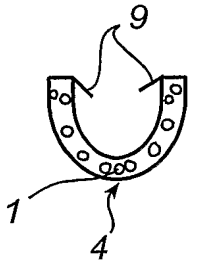


Fig. 20

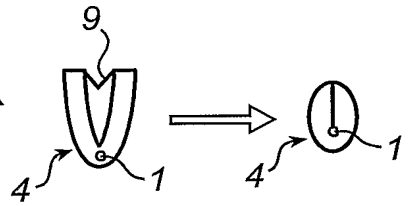


Fig. 21 Fig. 22

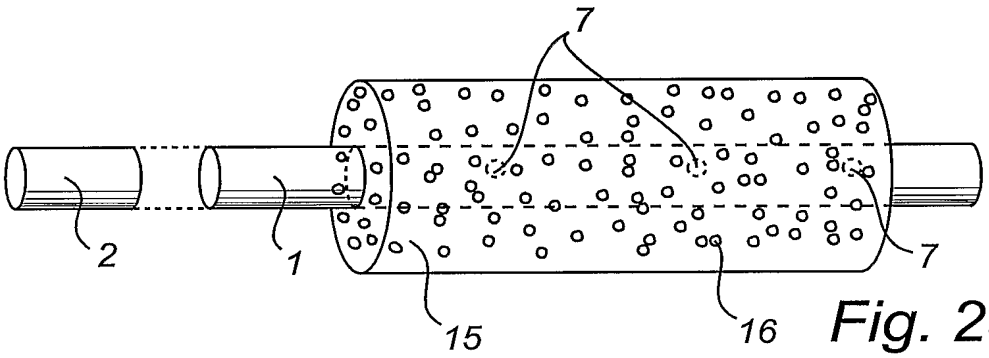


Fig. 23

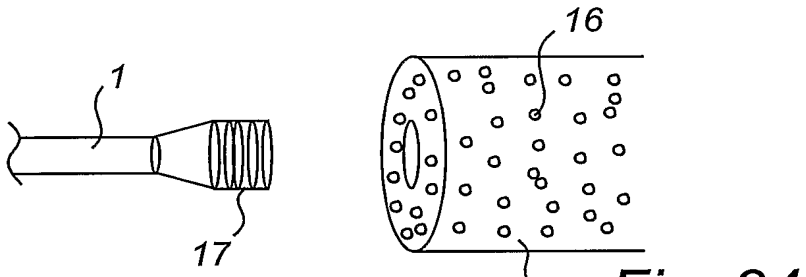


Fig. 24

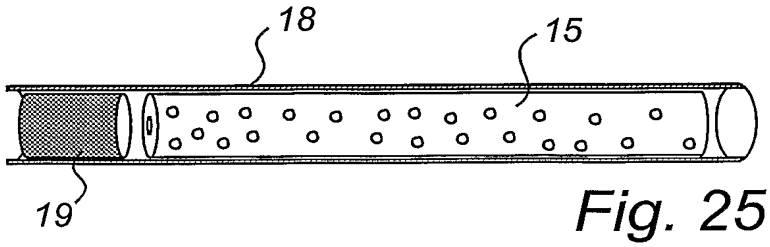


Fig. 25

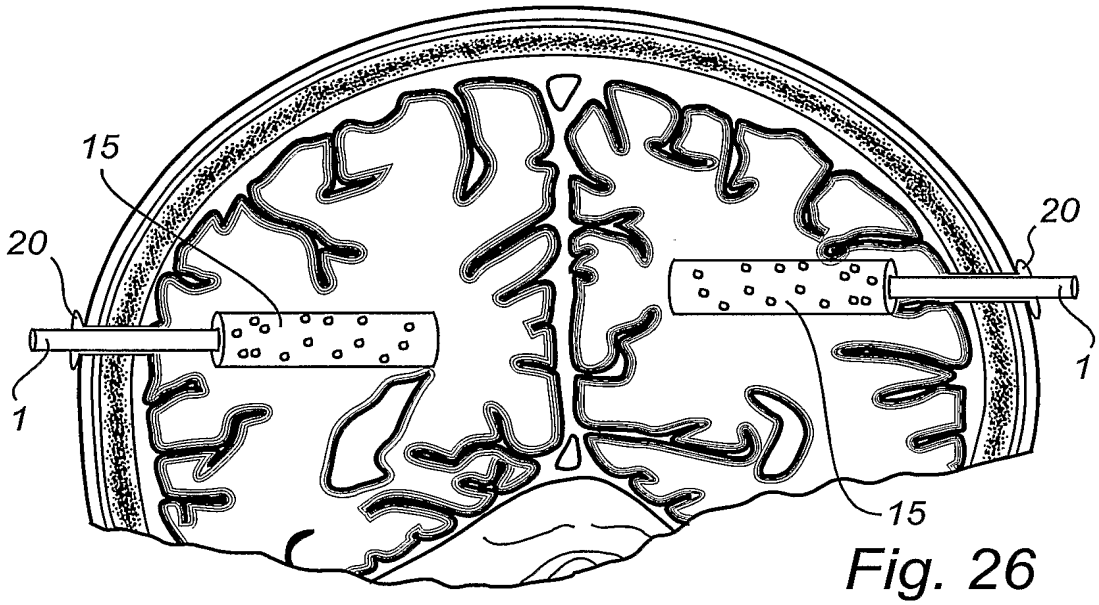


Fig. 26

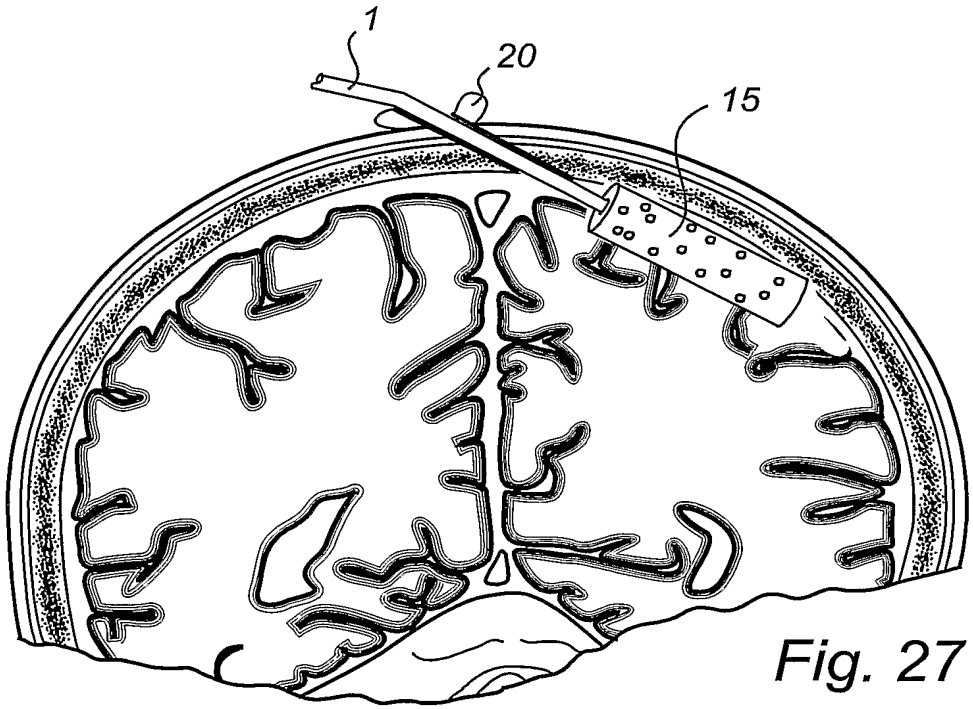


Fig. 27

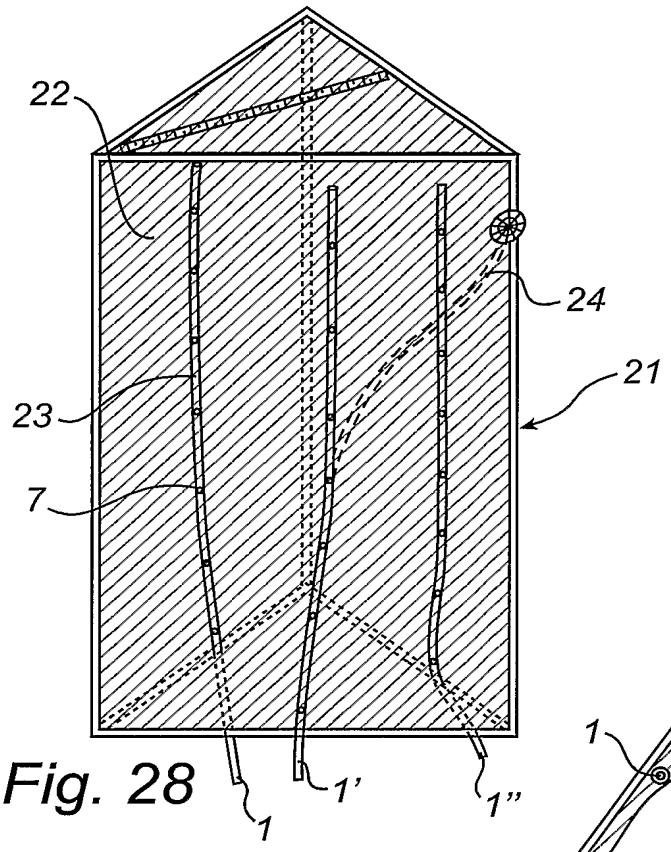


Fig. 28

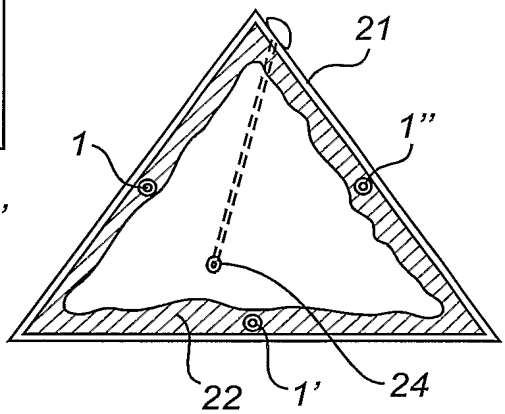


Fig. 29

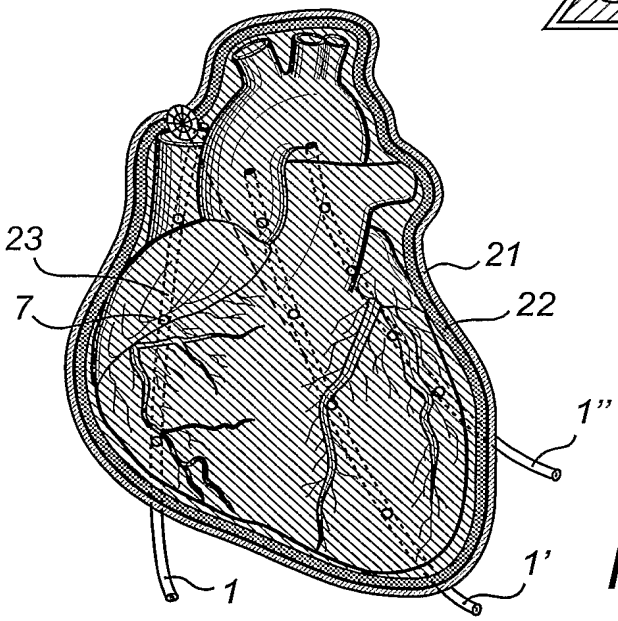


Fig. 30

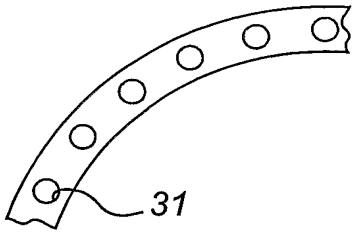


Fig. 31

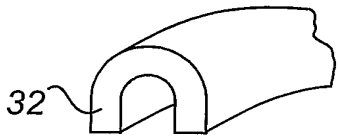


Fig. 32

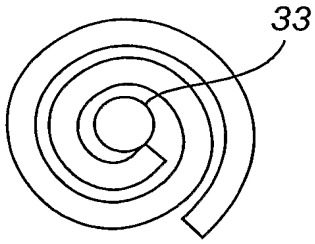


Fig. 33